09/013871

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L8	(heart adj lung adj machine)same (contact$ or admininist$)same (antibod$ or inhibit$ or antagonis$ or prevent$)	42	L8
L7	(heart adj lung adj machine)same (contact$ or admininist$)same (pharmaceutical$ or drug$)	3	L7
L6	(heart adj lung adj machine)same (contact$ or admininst$)	238	L6
L5	(heart adj lung adj machine)same (contact$ or admininst$) same (prior or before)	11	L5
L4	(heart adj lung adj machine)same (dose$ or dosage$)	82	L4
L3	(heart adj lung adj machine)same (dose$ or dosage$) same (pharmaceutical or drug$)	8	L3
L2	(heart adj lung adj machine)same (dose$ or dosage$)same (prior or before)	34	L2
DB=USPT; PLUR=YES; OP=ADJ			
L1	(heart adj lung adj machine)	1153	L1

END OF SEARCH HISTORY

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begin 5,73,155,399
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           $0.00    0.072 DialUnits File410
     $0.00  Estimated cost File410
     $0.02  TELNET
     $0.02  Estimated cost this search
     $0.34  Estimated total session cost   0.165 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2004/Jan W4
         (c) 2004 BIOSIS
  File  73:EMBASE  1974-2004/Jan W4
         (c) 2004 Elsevier Science B.V.
  File 155:MEDLINE(R)  1966-2004/Jan W4
         (c) format only 2004 The Dialog Corp.
*File 155: Medline is updating again (12-22-2003).
Please see HELP NEWS 154, for details.
  File 399:CA SEARCH(R)  1967-2004/UD=14006
         (c) 2004 American Chemical Society
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Alert feature enhanced for multiple files, etc. See HELP ALERT.

      Set  Items  Description
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? s (L(W)selectin or lam1 or lam(w)1 or leccam)(20n)(antibod?) and (sepsis or
infect?)(20n)(treat? or therap? or prevent? or inhibit? or suppress? or antagoni?)
Processing
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         1915004  L
           32749  SELECTIN
            8998  L(W)SELECTIN
             123  LAM1
            7696  LAM
         9562245  1
             366  LAM(W)1
              12  LECCAM
         1863528  ANTIBOD?
            1459  (((L(W)SELECTIN OR LAM1) OR LAM(W)1) OR
                  LECCAM)(20N)ANTIBOD?
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         3199032  INFECT?
         6334082  TREAT?
         5876934  THERAP?
         2039983  PREVENT?
         3909368  INHIBIT?
          790080  SUPPRESS?
         1033154  ANTAGONI?
          747800  (SEPSIS OR INFECT?)(20N)(((((TREAT? OR THERAP?) OR
                  PREVENT?) OR INHIBIT?) OR SUPPRESS?) OR ANTAGONI?)
      S1      38  (L(W)SELECTIN OR LAM1 OR LAM(W)1 OR
                  LECCAM)(20N)(ANTIBOD?) AND (SEPSIS OR
                  INFECT?)(20N)(TREAT? OR THERAP? OR PREVENT? OR INHIBIT?
                  OR SUPPRESS? OR ANTAGONI?)
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...completed examining records
      S2      23  RD S1 (unique items)
? t s2/7/all

 2/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0014060790 BIOSIS NO.: 200300019509
Evaluation of FIV protein-expressing VEE-replicon vaccine vectors in cats.
AUTHOR: Burkhard Mary Jo (Reprint); Valenski Loretta; Leavell Sarah; Dean Gregg A; Tompkins Wayne A F
AUTHOR ADDRESS: Department of Molecular Biomedical Sciences, North Carolina State University, Raleigh, NC, 27606, USA**USA
AUTHOR E-MAIL ADDRESS: maryjoburkhard@ncsu.edu
JOURNAL: Vaccine 21 (3-4): p258-268 13 December, 2002 2002
MEDIUM: print
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Venezuelan equine encephalitis (VEE) virus-replicon particles (VRP) were used to generate feline immunodeficiency virus (FIV) Gag- and ENV-expressing vaccine vectors. Serum and mucosal FIV-specific **antibody** was detected in cats immunized subcutaneously, once monthly for 5 months, with FIV-expressing VRP. Expansion of the CD8+ **L-selectin** negative phenotype and transient CD8+ noncytolytic suppressor activity were seen in cats immunized with FIV-expressing or control VRP. Despite induction of FIV-specific immune responses and nonspecific **suppressor** responses, all cats became **infected** following vaginal challenge with high dose, pathogenic cell-associated FIV-NCSU1 although relative early maintenance of CD4+ cells was seen in FIV-immunized cats.

2/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013902110 BIOSIS NO.: 200200495621
Cryptococcal glucuronoxylomannan inhibits adhesion of neutrophils to stimulated endothelium in vitro by affecting both neutrophils and endothelial cells
AUTHOR: Ellerbroek Pauline M (Reprint); Hoepelman Andy I M; Wolbers Floor; Zwaginga Jaap Jan; Coenjaerts Frank E J
AUTHOR ADDRESS: Division of Acute Internal Medicine and Infectious Diseases, University Medical Centre Utrecht, Heidelberglaan 100, 3508 GA, Utrecht, Netherlands**Netherlands
JOURNAL: Infection and Immunity 70 (9): p4762-4771 September, 2002 2002
MEDIUM: print
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Cryptococcal infections are often3pmn characterized by a paucity of leukocytes in the **infected** tissues. Previous research has shown that the capsular polysaccharide glucuronoxylomannan (GXM) **inhibits** leukocyte migration. In this study we investigated whether the capsular polysaccharide GXM affects the migration of neutrophils (polymorphonuclear leukocytes (PMN)) through the endothelium by interfering with adhesion in a static adhesion model. Pretreatment of PMN with GXM inhibited PMN adhesion to tumor necrosis factor alpha (TNF-alpha)-stimulated endothelium up to 44%. Treatment of TNF-alpha-stimulated endothelium with GXM led to a 27% decrease in PMN adhesion. GXM treatment of both PMN and endothelium did not have an additive inhibitory effect. We demonstrated that GXM-induced L-selectin shedding does not play an important role in the detected inhibition of adhesion. **L-selectin** was still present on PMN in sufficient

amounts after GXM treatment, since it could be further inhibited by blocking **antibodies**. Furthermore, blocking of GXM-related **L-selectin** shedding did not abolish the GXM-related inhibition of adhesion. GXM most likely exerts its effect on PMN by interfering with E-selectin-mediated binding. The use of blocking monoclonal antibodies against E-selectin, which was shown to decrease adhesion in the absence of GXM, did not cause additive inhibition of PMN adhesion after GXM pretreatment. The use of blocking antibodies also demonstrated that the inhibiting effect found after GXM treatment of endothelium probably involves interference with both intercellular adhesion molecule-1 and E-selectin binding.

2/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012138640 BIOSIS NO.: 199900398300
Redirected infection of directly biotinylated recombinant adenovirus vectors through cell surface receptors and antigens
AUTHOR: Smith Jeffrey S; Keller Jonathan R; Lohrey Nancy C; McCauslin Christine S; Ortiz Mariaestela; Cowan Kenneth; Spence Sally E (Reprint)
AUTHOR ADDRESS: National Cancer Institute-Frederick Cancer Research and Development Center, Building 560, Frederick, MD, 21702, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 96 (16): p8855-8860 Aug. 3, 1999 1999
MEDIUM: print
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The inability of adenovirus to infect primitive hematopoietic cells presents an obstacle to the use of adenovirus vectors for gene transfer to these cell types. Therefore, expanding the tropism of adenovirus vectors to unique cell surface antigens would be an important development for gene **therapy** protocols. In this study, we sought to redirect **infection** of adenovirus vectors to primitive human hematopoietic cells that universally express the c-Kit receptor on their cell surface. To accomplish this, a vector was constructed by covalently linking biotin molecules to recombinant adenovirus, followed by addition of the biotinylated ligand for the c-Kit receptor, stem cell factor (SCF), through an avidin bridge. Gene transfer was directed specifically to c-Kit-positive hematopoietic cell lines, resulting in up to a 2,440-fold increase in luciferase expression with frequencies equivalent to recombinant virus infection of permissive cells. Substitution of biotinylated **antibodies** directed against c-Kit, CD34 (binds **L-selectin**), and CD44 (hyaluronate receptor) receptors for biotinylated SCF resulted in 50-, 8-, and 260-fold increases in reporter gene expression, respectively, demonstrating that infection also could be redirected through antibody-antigen interactions and through antigens other than growth factor receptors. The versatility of this vector was demonstrated further by infection of primary T cells with vectors targeted with antibodies to CD44 (resting and activated T cells) and biotinylated IL-2 (activated T cells only). Taken together, directly biotinylated adenovirus vectors represent a versatile and efficient method for redirection of virus infection to specific cells.

2/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011393456 BIOSIS NO.: 199800187703

Antibody to E- and **L-selectin** does not prevent lung injury or mortality in septic baboons
AUTHOR: Carraway Martha Sue (Reprint); Welty-Wolf Karen E; Kantrow Stephen P; Huang Yu-Chin T; Simonson Steven G; Que Loretta G; Kishimoto Takashi K ; Piantadosi Claude A
AUTHOR ADDRESS: Div. Pulmonary Critical Care, P.O. Box 3315, Duke Univ. Med. Cent., Durham, NC 27710, USA**USA
JOURNAL: American Journal of Respiratory and Critical Care Medicine 157 (3 APRT 1): p938-949 March, 1998 1998
MEDIUM: print
ISSN: 1073-449X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recruitment of polymorphonuclear leukocytes (PMN) through upregulation of cellular adhesion molecules is a proposed mechanism of injury in sepsis and acute respiratory distress syndrome (ARDS). We hypothesized that pretreatment of baboons with a monoclonal **antibody** to human E- and **L-selectin** (EL-246) during sepsis would decrease PMN influx into tissues and result in less organ injury during gram-negative sepsis. We studied 14 anesthetized, ventilated adult baboons; six animals received 1 mg/kg of EL-246 before infusion of an LD100 of live Escherichia coli and six received the E. coli infusion without antibody therapy. Two other animals received 1 mg/kg of EL-246 intravenously without an infusion of bacteria. Intermittent measurements were made of circulatory pressures, cardiac output, urine output, arterial blood gases, ventilation:perfusion ratio (VA/Q), and hematologic status. The experiments were ended at 48 h or at the time of death. Tissues were harvested for pathology and biochemical measurements. The E. coli infusions were associated with a hyperdynamic state, pulmonary hypertension, systemic hypotension, decreased urine output (UOP), and metabolic acidosis. The antibody partly blocked PMN migration, but there were few significant physiologic or biochemical differences between the EL-246-treated and untreated animals. In the antibody-treated animals, UOP was decreased, metabolic acidosis was worsened, and median survival time was decreased significantly. We conclude that **treatment** with an **antibody** to E- and **L-selectin** in gram-negative **sepsis** does not improve gas exchange or protect against lung injury, and is associated with decreased survival time in primates.

2/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010050383 BIOSIS NO.: 199598518216
Differential effects of monoclonal antibody blockade of adhesion molecules on in vivo susceptibility to soft tissue infection
AUTHOR: Garcia Nilda; Mileski W J (Reprint); Lipsky Peter
AUTHOR ADDRESS: Dep. Surgery, Univ. Texas Southwestern Med. Cent., 5323 Harry Hines Blvd., Dallas, TX 75235-9031, USA**USA
JOURNAL: Infection and Immunity 63 (10): p3816-3819 1995 1995
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Leukocyte adherence to endothelial cells has been implicated in the pathogenesis of microvascular injury as well as in host defense against various **infectious** microorganisms. Administration of monoclonal antibodies directed against the beta chain of the leukocyte integrins **inhibits** leukocyte-endothelial-cell adherence and has

been reported to modulate ischemia-reperfusion and inflammatory injury. However, such **inhibition** of adhesion molecule function adversely affects resistance to **infection**. The following studies were carried out to determine whether monoclonal **antibodies** to other adhesion molecules, including **L-selectin** (CD62L), and CD11a (the ot chain of LFA-1), also increase susceptibility to infection. New Zealand White rabbits were shaved and given subcutaneous injections on their dorsa with 10-9 CFU of Staphylococcus aureus ATCC 25923 at two sites and with 10-8 CFU at two sites. A second set of rabbits were given subcutaneous injections with 10-8 CFU of P. aeruginosa ATCC 27853 at two sites and with 10-7 CFUs at two sites. The animals were monitored for 1 week. There were three blinded experimental groups: controls given saline and two groups given blocking monoclonal **antibodies** to either **L-selectin** (Dreg-200) or CD11a (R7.1). In contrast to monoclonal **antibodies** to CD18, none of the monoclonal **antibodies** significantly increased the risk of abscess formation by S. aureus, although inhibition of CD11a increased the rate of abscess formation by P. aeruginosa.

2/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009908811 BIOSIS NO.: 199598376644
Subverting lymph node trafficking by treatment with the mel-14 monoclonal **antibody** to **L-selectin** does not prevent an effective host response to Sendai virus
AUTHOR: Hou Sam; Hyland Lisa; Bradley Linda M; Watson Susan R; Doherty Peter C
AUTHOR ADDRESS: St. Jude Children's Res. Hosp., 332 North Lauderdale, Memphis, TN 38105, USA**USA
JOURNAL: Journal of Immunology 155 (1): p252-258 1995 1995
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A single 250-mu-g dose of the Mel-14 mAb to L-selectin greatly diminished the extent of L-selectin expression on lymphocytes and decreased (60 to 90%) the massive cellular recruitment to the cervical and mediastinal lymph nodes that follows intranasal infection of naive C57BL/6 mice with Sendai virus. The numbers of CD8+ CTL precursors in the mediastinal lymph nodes were considerably reduced on day 7, when compared with virus-infected mice given a control rat IgG2a, but potent CTL effectors were present in the lungs of both groups by day 10 after infection, and the overall magnitude of CTL precursor generation was not obviously compromised. The early dominance of Sendai virus-specific IgM Ab-forming cells was prolonged in the Mel-14-treated mice, whereas plasma cells producing virus-specific IgA were abnormally prominent in the lymph nodes but not in the spleen. The kinetics of virus-specific Ab-forming cells generation and the serum Ab response for the various IgG isotypes were also delayed. Thus, though L-selectin is clearly important for the localization of naive lymphocytes to regional lymph nodes, the Mel-14-**treated** mouse can still deal effectively with a virus that causes productive **infection** only in the respiratory tract. The spleen, where L-selectin does not determine lymphocyte trafficking, is a major site for the compensatory T cell and B cell responses.

2/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009308126 BIOSIS NO.: 199497329411
Effect of **inhibiting** leukocyte integrin (CD18) and selectin (L-selectin) on susceptibility to **infection** with Pseudomonas aeruginosa
AUTHOR: Garcia Nilda M; Mileski William J (Reprint); Sikes Patricia; Atiles Luis; Lightfoot Ellis; Lipsky Peter; Baxter Charles
AUTHOR ADDRESS: Delp. Surg., Univ. Texas Southwestern Med. Cent., 5323 Harry Hines Blvd., Dallas, TX 75235-9031, USA**USA
JOURNAL: Journal of Trauma 36 (5): p714-719 1994 1994
ISSN: 0022-5282
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Leukocyte (WBC) adherence to endothelial cells has been implicated in the pathogenesis of microvascular injury. The process of leukocyte adherence is mediated by both the integrin and selectin families of molecules, and their interaction with specific endothelial ligands. **Antibodies** directed against the leukocyte integrin CD18 and **L-selectin** have been developed and functionally inhibit leukocyte adherence in models of inflammatory injury. We asked the question: Does inhibition of leukocyte adherence by administration of monoclonal **antibody** directed against either CD18, integrins (R15.7, R7.1) or against **L-selectin** (DREG 200) increase susceptibility to infection? New Zealand white rabbits were shaved and injected subcutaneously on their dorsum with Pseudomonas aeruginosa (ATCC 27853) at two sites each of 10-8 and 10-7 colony forming units. Animals were monitored with daily determination of weight, temperature, WBC counts, hematocrit, and killed at 1 week for determination of abscess formation. There were four blinded experimental groups: (1) Saline (2 mL/kg); (2) DREG 200 (2 mg/kg); (3) R7.1 (2 mg/kg); or (4) R15.7 (2 mg/kg). At the 10-7 and 10-8 injection sites the R15.7 group had an increased rate and size of abscess formation compared with controls. The R7.1 group had an increased rate at the 10-8 injection site. There was no significant difference in the percentage of the abscess formation or mean area between the controls and DREG 200-**treated** groups. We conclude that giving **antibody** to CD18 increased susceptibility to **infection** while giving **antibody** to **L-selectin** does not.

2/7/8 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11767848 EMBASE No: 2002340755
Preventive effect of sulphated colominic acid on P-selectin-dependent infiltration of macrophages in experimentally induced crescentic glomerulonephritis
Ogawa D.; Shikata K.; Matsuda M.; Okada S.; Wada J.; Yamaguchi S.; Suzuki Y.; Miyasaka M.; Tojo S.; Makino H.
Dr. K. Shikata, Department of Medicine III, Okayama University Medical School, 2-5-1 Shikata-cho, Okayama 700-8558 Japan
AUTHOR EMAIL: shikata@md.okayama-u.ac.jp
Clinical and Experimental Immunology (CLIN. EXP. IMMUNOL.) (United Kingdom) 2002, 129/1 (43-53)
CODEN: CEXIA ISSN: 0009-9104
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 44

Leucocytes infiltrate into renal tissue and are involved in the pathogenesis of crescentic glomerulonephritis. The initial event in the process of leucocyte infiltration is characterized by selectin-mediated

leucocyte rolling on endothelial surface. Role of selectins in pathogenesis of glomerulonephritis has still been controversial. Sulphated glycolipids and sulphated polysaccharides interfere with the binding of P- and L-selectin with carbohydrate ligands on endothelial cells or on leucocytes. Here we evaluated the role of selectins and the preventive effects of sulphated colominic acid (SCA), a synthetic sulphated polysaccharide, on experimental crescentic glomerulonephritis in Wistar-Kyoto (WKY) rats. Crescentic glomerulonephritis was induced by injection of nephrotoxic serum (NTS) in WKY rats. Rats subsequently received intraperitoneal injection of saline, neutralizing or non-neutralizing monoclonal **antibody** (mAb) to rat P-selectin and **L-selectin**, SCA (5 or 10 mg/kg/day) or nonsulphated colominic acid (CA) (10 mg/kg/day) for 2 weeks. Localization of P-, E-selectin, ligands for L-selectin and intraglomerular leucocytes was examined by immunohistochemistry. Gene expression of platelet-derived growth factor (PDGF) B chain in glomeruli was quantified using real-time RT-PCR. P-selectin was highly expressed on glomerular endothelial cells after injection of NTS, whereas E-selectin and L-selectin ligands were not detected. Anti-P-selectin mAb, but not anti-L-selectin mAb, significantly reduced glomerular infiltration of macrophages, crescent formation, and proteinuria. SCA also reduced proteinuria, macrophage infiltration, and crescent formation in a dose-dependent manner. Furthermore, SCA suppressed gene expression of PDGF B chain in glomeruli. Our results indicate that P-selectin partially mediate glomerular infiltration of macrophage in experimental crescentic glomerulonephritis. Moreover, SCA may inhibit intraglomerular infiltration of macrophages by interfering with P-selectin-dependent adhesion pathway, and progression of experimental crescentic glomerulonephritis.

2/7/9 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11409825 EMBASE No: 2001424385
Immunopathology of Bartonella vinsonii (berkhoffii) in experimentally infected dogs
Pappalardo B.L.; Brown T.T.; Tompkins M.; Breitschwerdt E.B.
B.L. Pappalardo, Blood Center of the Pacipic, 270 Masonic Avenue, San Francisco, CA 94118 United States
Veterinary Immunology and Immunopathology (VET. IMMUNOL. IMMUNOPATHOL.) (Netherlands) 2001, 83/3-4 (125-147)
CODEN: VIIMD ISSN: 0165-2427
PUBLISHER ITEM IDENTIFIER: S0165242701003725
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 44

Following natural infection with Bartonella, dogs and humans develop comparable disease manifestations including endocarditis, peliosis hepatis, and granulomatous disease. As the immunologic response to infection in these hosts has not been clearly established, data presented here was derived from the experimental infection of six specific pathogen free (SPF) beagles with a known pathogenic strain of Bartonella. Six dogs were inoculated intravenously with 10SUP9cfu of B. vinsonii ssp. berkhoffii and six control dogs were injected intravenously with an equivalent volume of sterile saline. Despite production of substantial levels of specific antibody, blood culture and molecular analyses indicated that Bartonella established chronic infection in these dogs. Flow cytometric analysis of monocytes indicated impaired bacterial phagocytosis during chronic Bartonella infection. There was also a sustained decrease in the percentage of CD8+ lymphocytes in the peripheral blood. Moreover, modulation of adhesion molecule expression (downregulation of L-selectin, VLA-4, and LFA-1) on CD8+ lymphocytes suggested quantitative and qualitative impairment of this cell subset in Bartonella-infected dogs. When compared

with control dogs, flow cytometric analysis of lymph node (LN) cells from B. vinsonii infected dogs revealed an expanded population of CD4+ T cells with an apparent naive phenotype (CD45RA+/CD62L+/CD49DSUBdim). However, fewer B cells from infected dogs expressed cell-surface MHC II, implicating impaired antigen presentation to helper T cells within LN. Taken together, results from this study indicate that B. vinsonii establishes chronic **infection** in dogs which may result in immune **suppression** characterized by defects in monocytic phagocytosis, an impaired subset of CD8+ T lymphocytes, and impaired antigen presentation within LN.

2/7/10 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

11260664 EMBASE No: 2001275317
The comparative efficacy of CTLA-4 and L-selectin targeted DNA vaccines in mice and sheep
Drew D.R.; Boyle J.S.; Lew A.M.; Lightowlers M.W.; Chaplin P.J.; Strugnell R.A.
D.R. Drew, Walter/Eliza Hall Inst. of Med. Res., Royal Melbourne Hospital, Melbourne, Vic. 3050 Australia
AUTHOR EMAIL: drew@wehi.edu.au
Vaccine (VACCINE) (United Kingdom) 14 AUG 2001, 19/31 (4417-4428)
CODEN: VACCD ISSN: 0264-410X
PUBLISHER ITEM IDENTIFIER: S0264410X01001967
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 46

The access of antigens to antigen presenting cells (APCs) appears to be a rate-limiting step in the generation of immune responses to DNA vaccines. The cytotoxic T lymphocyte antigen 4 (CTLA-4) and L-selectin represent attractive ligands for use in the targeting of antigen to APCs and lymph nodes. CTLA-4 binds with high affinity to the B7 membrane antigen on APCs, while L-selectin functions as a lymphocyte homing marker and binds to CD34 on the surface of high endothelial venule cells. DNA vaccines encoding human immunoglobulin (HIg), fused to either CTLA-4 or **L-selectin**, have been shown to generate up to 10,000-fold higher anti-HIg **antibody** responses than DNA vaccines encoding HIg alone. In this study, the ability of CTLA-4 or **L-selectin** mediated targeting to enhance the humoral immune response to an alternate vaccine antigen was investigated. DNA vaccines encoding CTLA-4-HIg and L-selectin-HIg fused to the host-protective 45W antigen from Taenia ovis were constructed. In BALB/c mice, the **L-selectin** targeted vaccine did not improve either the magnitude or speed of **antibody** responses of vaccinated mice. In contrast, the CTLA-4 targeted DNA vaccine generated 45W-specific antibody responses which were up to 30-fold higher than those achieved with non-targeted DNA vaccination. The kinetic of the antibody response generated following CTLA-4 targeted DNA vaccination was also significantly faster than that achieved with non-targeted DNA vaccination, or with adjuvanted protein vaccination. Vaccination of outbred sheep with DNA vaccines expressing either murine or ovine CTLA-4 targeted antigen failed to enhance immune responses. These findings indicate that CTLA-4 targeting may find application in the improvement of DNA vaccines, but requires further development for applications in large animal species. (c) 2001 Published by Elsevier Science Ltd.

2/7/11 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

06305350 EMBASE No: 1995342203
Sepsis-induced acute lung injury is attenuated by selectin blockade following the onset of sepsis
Ridings P.C.; Bloomfield G.L.; Holloway S.; Windsor A.C.J.; Jutila M.A.; Fowler III A.A.; Sugerman H.J.; Barie P.S.; Hotchkiss R.S.
Department of Surgery, Medical College of Virginia, Box 980519,Richmond, VA 23298 United States
Archives of Surgery (ARCH. SURG.) (United States) 1995, 130/11 (1199-1208)
CODEN: ARSUA ISSN: 0004-0010
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Objective: To determine the effect of infusion with a dual-binding **antibody** to E- and **L-selectin**, EL-246, in a post onset model of sepsis. Design: Nonrandomized controlled study. Study Subjects: Young Yorkshire swine. Interventions: Three groups were studied. Controls (n=8) received saline solution only. Untreated animals with **sepsis** (n=8) received a 1-hour intravenous infusion of live Pseudomonas aeruginosa. Animals **treated** with EL- 246 (n=6) received the same bacterial infusion and a 2-mg/kg bolus of EL-246 at 30 minutes. Outcome Measures: Systemic and pulmonary hemodynamics, arterial blood gas determination, bronchoalveolar lavage protein and neutrophil content, neutrophil integrin and selectin expression, neutrophil oxidant burst, and organ myeloperoxidase content. Results: Treatment with EL- 246 significantly reduced lung injury, as indicated by improved bronchoalveolar lavage protein and neutrophil content, resulting in a significant improvement in arterial oxygenation. This reduction in lung injury was produced by a reduction in lung myeloperoxidase content. **Treatment** with EL-246 failed to **prevent** the development of pulmonary hypertension and systemic hypotension. Neutrophils from animals with **sepsis** exhibited significant activation and upregulation of CD18, shedding of L-selectin, and production of increased levels of oxidants compared with controls. Conclusions: **Treatment** of animals with EL-246 soon the onset of **sepsis** produced significant protection against acute lung injury but failed to attenuate hemodynamic derangements associated with sepsis.

2/7/12 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

05755719 EMBASE No: 1994168827
Modulation of host response to Escherichia coli O157:H7 infection by anti- CD18 antibody in rabbits
Elliott E.; Li Z.; Bell C.; Stiel D.; Buret A.; Wallace J.; Brzuszczak I.; O'Loughlin E.
Department of Pediatrics, John Hunter Hospital, Lookout Road,New Lambton, NSW 2305 Australia
Gastroenterology (GASTROENTEROLOGY) (United States) 1994, 106/6 (1554-1561)
CODEN: GASTA ISSN: 0016-5085
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Background/Aims: Escherichia coli O157:H7 infection induces diarrhea, severe colitis, and colonic electrolyte transport abnormalities characterized by decreased Na absorption and Cl secretion. The aim of this study was to examine the role of the host inflammatory response in inducing distal colonic transport changes during infection with E. coli O157:H7. Methods: New Zealand white rabbits aged 10 days were infected with E. coli O157:H7 strain EDL933 (plasmidsup +, verotoxin 1sup +, verotoxin 2sup +). Studies were performed daily from day 1 to day 5 postinfection and compared

with uninfected controls (10 days old). Distal colonic ion transport was studied in vitro under short- circuited conditions in Ussing chambers, and tissue inflammation was assessed by mucosal myeloperoxidase activities and mucosal neutrophil (polymorphonuclear neutrophil (PMN)) counts. In a second study, PMN infiltration was inhibited by an anti-CD18 (leukocyte adhesion molecule) monoclonal antibody, IBinf 4, and histology and transport were studied on day 5 postinfection. Results: **Infection** with O157:H7 induced diarrhea and **inhibition** of Na absorption by day 3. Cl secretion occurred on day 5, coincident with tissue infiltration with PMN. Pretreatment with IBinf 4 **prevented** histological damage and tissue infiltration with PMN, and it **inhibited** the transport abnormalities induced by **infection** alone. Conclusions: **Infection** with O157:H7 reduces Na absorption and stimulates Cl secretion in the distal colon. Disruption of the epithelium and changes in colonic electrolyte transport during enterohemorrhagic E. coli are mediated by the host inflammatory response.

2/7/13 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

05441183 EMBASE No: 1993209282
Pharmacologic approaches to respiratory failure
Hudson L.D.; Dantzker D.R.
Harborview Medical Center,Seattle, WA 98104 United States
Respiratory Care (RESPIR. CARE) (United States) 1993, 38/7 (754-768)
CODEN: RECAC ISSN: 0098-9142
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH

2/7/14 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

05301680 EMBASE No: 1993069765
Pathogenesis of multiple sclerosis - The immune diathesis and the role of viruses
Allen I.; Brankin B.
Division of Neuropathology, Institute of Pathology, Queen's University, Grosvenor Road,Belfast BT12 6BL United Kingdom
Journal of Neuropathology and Experimental Neurology (J. NEUROPATHOL. EXP. NEUROL.) (United States) 1993, 52/2 (95-105)
CODEN: JNENA ISSN: 0022-3069
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Although the evidence of involvement of viruses in the pathogenesis of MS is largely circumstantial, the pattern of association is constant, with little evidence for direct viral infection of the CNS but with a consistent immune response to several common viruses. In parallel with these studies, epidemiological studies, while indicating genetic predisposition, favor an environmental pathogenetic factor and experimental models indicate that viruses can induce demyelination either by oligodendrolysis or by a variety of immune mechanisms with or without persistence in the CNS. In elucidating the pathogenesis of MS, the challenge is to understand the basis of the immune abnormalities, with intrathecal synthesis of viral antibodies and abnormal immune responses to some viruses, and to relate these to the MRI abnormalities which indicate periodic BBB breakdown. There is strong evidence that the breakdown is associated with inflammation (82) and that cytokines, particularly TNF, may play a role in demyelination (15, 83). In conclusion, therefore, several factors are probably key in our understanding of MS. These include: (i) the genetic control of the immune

system and its interaction with viral antigen; (ii) related effects on cerebral endothelium including cytokine and adhesion molecule regulation; and (iii) associated glial and axonal responses. Such an approach to the pathogenesis of MS may not identify a specific cause. It may, however, indicate that a pathological cascade can be 'triggered' by several common viral **infections** and that **therapy** can be used to intervene at several points in the pathological response.

2/7/15 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11936756 99380593 PMID: 10449768
Ligation of the CD4 receptor induces activation-independent down-regulation of L-selectin.
Marschner S; Freiberg B A; Kupfer A; Hunig T; Finkel T H
Division of Basic Sciences, Department of Pediatrics, National Jewish Medical and Research Center, Denver, CO 80206, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 17 1999, 96 (17) p9763-8, ISSN 0027-8424 Journal Code: 7505876
Contract/Grant No.: RO1 AI 40003; AI; NIAID; RO1 AI23764D; AI; NIAID; RO1 AI35513; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Lymphocyte circulation plays an important role in the generation of a specific immune response. Mature lymphocytes continuously circulate between blood and lymph, entering the lymphoid tissue via high endothelial venules. Trafficking across high endothelial venules of peripheral lymph nodes (PLN) depends on the expression of L-selectin. It has been shown that L-selectin is rapidly cleaved from the surface by a metalloproteinase after in vitro activation. Here, we show that ligation of CD4, without ligation of the T cell receptor for antigen, causes down-regulation of L-selectin on T helper cells. This down-regulation is caused by proteolytic cleavage by a metalloproteinase and is reversible by the addition of hydroxamic acid-based metalloproteinase inhibitors. We show that in vivo down-regulation of L-selectin in huCD4tg mice by mAb reduces the homing of lymphocytes to PLN in adoptive transfer experiments. Because CD4 is a coreceptor for HIV-1, the down-regulation of L-selectin induced by CD4 ligation could play a role in the pathogenesis of AIDS. We provide evidence that CD4 ligation by HIV-1 induces metalloproteinase-dependent L-selectin down-regulation. Reduced levels of L-selectin expression might contribute to immune deficiency in individuals **infected** with HIV by **inhibiting** T cell redistribution and decreasing the probability of an encounter between specific lymphocytes and viral antigens in PLN.
Record Date Created: 19990909
Record Date Completed: 19990909

2/7/16 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10584226 96399086 PMID: 8805657
L-selectin (CD62L) blockade does not impair peritoneal neutrophil emigration or subcutaneous host defense to bacteria in rabbits.
Sharar S R; Chapman N N; Flaherty L C; Harlan J M; Tedder T F; Winn R K
Department of Anesthesiology, University of Washington School of Medicine, Seattle 98195, USA.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Sep 15 1996, 157 (6) p2555-63, ISSN 0022-1767 Journal Code: 2985117R

Contract/Grant No.: CA54464; CA; NCI; GM42686; GM; NIGMS; HL50985; HL; NHLBI; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Neutrophil (PMN) recruitment into systemic inflammatory sites in vivo is thought to be initiated by selectin-mediated endothelial adherence. We explored the role of L-selectin (CD62L) in leukocyte emigration following instillation of bacteria into the peritoneum or s.c. skin in rabbits. Pretreatment with blocking mAb against L-selectin (LAM1.3) reduced peritoneal PMN emigration 4 h after i.p. inoculation with 10(10) CFU of Escherichia coli by only 17% compared with animals receiving a nonblocking L-selectin mAb (LAM1.14). Peritoneal PMNs from saline-treated rabbits demonstrated a complete absence of L-selectin, whereas those from LAM1.3-treated animals retained 43% of their baseline L-selectin expression. This suggests that L-selectin shedding is not a requisite event for PMN emigration under these conditions. In rabbits given s.c. inoculations with either Staphylococcus aureus or E coli, pretreatment with mAb LAM1.3 did not significantly impair PMN emigration at 24 h, nor increase the incidence, size, or associated mortality of resulting abscesses at 7 days compared with animals receiving nonblocking mAb LAM1.14. We conclude that: 1) mAb blockade of L-selectin in vivo only modestly affects acute, E. coli-induced peritoneal PMN emigration; and 2) L-selectin blockade does not increase infectious sequelae associated with s.c. bacterial inoculation. These findings of only mildly reduced PMN emigration into the peritoneum and no alteration in s.c. host defense differ from those reported with L-selectin blockade under other, nonbacterial inflammatory conditions, and suggest that redundant selectin-mediated mechanisms (P- and E-selectin) are sufficient for normal PMN emigration in response to bacterial stimulation.

Record Date Created: 19961212
Record Date Completed: 19961212

2/7/17 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10334361 96136667 PMID: 8533991
Regulation of neutrophil adhesion molecules and shedding of Staphylococcus aureus in milk of cortisol- and dexamethasone-treated cows.
Burton J L; Kehrli M E
USDA, Agricultural Research Service, National Animal Disease Center, Ames, IA 50010-0070, USA.
American journal of veterinary research (UNITED STATES) Aug 1995, 56 (8) p997-1006, ISSN 0002-9645 Journal Code: 0375011
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The effects of 3 days of glucocorticoid administration on bovine blood neutrophil expression of L-selectin and CD18, and on the health status of mammary glands subclinically infected with Staphylococcus aureus were measured in 9 lactating Holsteins. The experiment was a 3 x 3 Latin square cross-over design, with 3 glucocorticoid treatments switched among groups of 3 cows/treatment during 3 periods. Treatments consisted of a vehicle (control, 10 ml of excipient/cow/d), cortisol (7.5, 15, and 7.5 mg/cow on days 1, 2, and 3, respectively), and dexamethasone (0.04 mg/kg of body weight/cow/d for total daily dosages that ranged from 21.6 to 33.2 mg). Blood samples for immunostaining and flow cytometric analysis of L-selectin and CD18 and leukograms, as well as foremilk samples for determination of S aureus shedding, somatic cell counts, protein and fat percentages, and daily milk yields were collected repeatedly before, during, and after

treatment days. Dexamethasone caused a profound, acute, short-lived down-regulation of L-selectin on neutrophils, which correlated in time to leukocytosis, mature and immature neutrophilias, increased shedding of S aureus in infected glands, and onset of high percentages of fat and protein and decreased milk yields. Dexamethasone also caused profound but delayed down-regulation of neutrophil CD18, which reached nadir simultaneously with reappearance of L-selectin-bearing neutrophils, normalized blood neutrophil counts, markedly high foremilk somatic cell counts and protein percentage, decreased S aureus shedding in milk, and finally, expression of clinical mastitis in some infected quarters. Each of these variables had returned to control (vehicle) values by the ninth (and last) sample collection day. Although cortisol treatment also decreased expression of L-selectin and CD18 on neutrophils, dosages used in this study were not sufficient to alter the number of circulating cells or to convert subclinical mammary gland infections to clinical mastitis. These results suggest that mammary gland health status can be altered by sudden exposure of blood neutrophils to glucocorticoids, because these steroid hormones caused profound down-regulation of the adhesion molecules that direct neutrophil margination and migration through the vascular endothelium. The results also reinforce the potential disease risk of **treating infected** animals with potent synthetic glucocorticoids, such as dexamethasone.

Record Date Created: 19960130

Record Date Completed: 19960130

2/7/18 (Item 4 from file: 155)

09792909 21599925 PMID: 11736952

An in vitro system for testing leucocyte and leukaemic cell line adhesion to synthetic fibres.

Barbe L L; Boval B M; Wautier M P; Wautier J L

Laboratoire de Biologie Vasculaire et Cellulaire, Paris, and Institut National de la Transfusion Sanguine (INTS), and Institut National de la Recherche Medicale (INSERM) U76, Paris, France.

British journal of haematology (England) Dec 2001, 115 (3) p664-71, ISSN 0007-1048 Journal Code: 0372544

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Leucocyte adhesion is an important phenomenon in antimicrobial defence, inflammation and immunological mechanisms and has been shown to be dependent upon specialized adhesion molecules. To **prevent** side-effects related to blood transfusion (e.g. anti-human leucocyte antigen immunization and transmission of **infectious** agents) leucocyte reduction of blood products is now systematically performed in various countries. The most common system used for leucoreduction is blood filtration. For further understanding of the mechanisms responsible for the interaction between leucocytes and the fibres present in filters we used a flow chamber to study the adhesion of leucocytes and leukaemic cell lines to different types of fibre. Adhesion was quantified using video-microscopy and computer image analysis. Our results demonstrate that adhesion to filter fibres was dependent on the expression of beta2-integrins CD11--CD18 and was inhibited by anti-CD18. The amount of fibres present, their spatial arrangement and the physicochemical characteristics of the fibres were important factors in leucocyte adhesion. Leucocyte adhesion was the highest to polyethylene terephthalate (PET) and polyimide fibres. Lymphocytes or lymphocytic cell lines were poorly adherent to PET fibres. The retaining capacity of leucocyte filters can be improved by taking into account the different parameters for the design of new filters

Record Date Created: 20011212

Record Date Completed: 20020107

2/7/19 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09097417 20395239 PMID: 10940890
Maintenance of IL-12-responsive CD4+ T cells during a Th2 response in Leishmania major-infected mice.
Hondowicz B D; Park A Y; Elloso M M; Scott P
University of Pennsylvania, School of Veterinary Medicine, Philadelphia 19104, USA.
European journal of immunology (GERMANY) Jul 2000, 30 (7) p2007-14, ISSN 0014-2980 Journal Code: 1273201
Contract/Grant No.: AI35914; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BALB/c and anti-IL-12-**treated** C3H mice **infected** with Leishmania major develop a Th2 cell response. However, in contrast to BALB/c mice, C3H mice **treated** transiently with an anti-IL-12 monoclonal antibody switch from a Th2 to a Th1 response and resolve their lesions once treatment is terminated. We report here that the critical difference in the Th2 response between BALB/c and C3H mice is in their ability to respond to IL-12. Thus, C3H mice with a Th2 response maintain a CD4+ T cell population that expresses IL-12 receptor beta1 and beta2 mRNA and produces IFN-gamma after exposure to IL-12. These results indicate that Th2 cell populations from different genetic backgrounds differ in their stability, and that this difference can be related to differential regulation of the IL-12 receptor.
Record Date Created: 20000913
Record Date Completed: 20000913

2/7/20 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08974648 20265297 PMID: 10807017
Proinflammatory cytokines increase in **sepsis** after anti-adhesion molecule **therapy**.
Welty-Wolf K E; Carraway M S; Ghio A; Kantrow S P; Huang Y C; Piantadosi C A
Department of Medicine, Durham VA Medical Center, North Carolina 27710, USA.
Shock (Augusta, Ga.) (UNITED STATES) May 2000, 13 (5) p404-9, ISSN 1073-2322 Journal Code: 9421564
Contract/Grant No.: P01 HL 31992; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Cytokine mediators and leukocyte-endothelial cell adhesion molecules are critical and interdependent components of the acute inflammatory response in sepsis. We hypothesized that the administration of monoclonal **antibodies** to intercellular adhesion molecule-1 (CD54) or E- and **L-selectin** (CD62E/L) would decrease serum levels of the proinflammatory cytokines interleukin-1beta (IL-1), IL-6, and IL-8 and tumor necrosis factor receptor (TNFR-1) in baboons during sepsis. Adult male baboons received infusions of 1 x 10(9) colony forming units (CFU)/kg heat-killed Escherichia coli (E. coli) followed 12 h later by live E. coli (1 x 10(10) CFU/kg). At the time of live bacterial infusion, six septic animals were treated with a monoclonal antibody to CD54 and six with an

antibody to CD62E and L (1 mg/kg). Eight untreated septic animals served as controls. Sequentially drawn serum samples were assayed for IL-1, IL-6, IL-8, and TNFR-1 using enzyme-linked immunoassay (ELISA). Data were compared using Mann-Whitney U tests and Chi-square analyses. Median survival was decreased in both treatment groups compared to controls ($P < 0.05$). Peak IL-1 level was higher than controls in septic animals treated with anti-CD54 but not anti-CD62E/L ($P < 0.05$, P = NS, respectively). Elevations in IL-6, IL-8, and TNFR-1 were increased and prolonged in both antibody treated groups compared to controls ($P < 0.05$). These results provide the first in vivo evidence that leukocyte-endothelial adhesion molecules CD54 and CD62E/L regulate cytokine production in sepsis.
Record Date Created: 20000725
Record Date Completed: 20000725

2/7/21 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08634654 95323181 PMID: 7541277
A dual-binding **antibody** to E- and **L-selectin** attenuates sepsis-induced lung injury.
Ridings P C; Windsor A C; Jutila M A; Blocher C R; Fisher B J; Sholley M M; Sugerman H J; Fowler A A
Department of Surgery, Medical College of Virginia, Virginia Commonwealth University, Richmond, USA.
American journal of respiratory and critical care medicine (UNITED STATES) Jul 1995, 152 (1) p247-53, ISSN 1073-449X Journal Code: 9421642
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Many studies indicate a pivotal role for neutrophil adhesion in sepsis-associated lung injury. Neutrophil adhesion to endothelium depends on activation and expression of selectin and integrin adhesion receptors. We studied the effects of pretreatment with a dual-binding porcine anti-E- and anti-**L-selectin** monoclonal **antibody** (EL-246) on a porcine model of sepsis-induced lung injury. Four groups were studied for 5 h. Group 1 (control animals) received intravenous saline only. Group 2 (septic) received a 1-h infusion of Pseudomonas aeruginosa. Group 3 (EL-246 pretreatment) received EL-246 (1 mg/kg) prior to Pseudomonas infusion. Group 4 (EL-246 controls) received EL-246 infusion only. Group 2 animals showed rapid, significant decline in arterial pH and oxygen tension whereas, in Group 3, physiologic deterioration was significantly attenuated. Bronchoalveolar lavage at 5 h showed a significant increase in neutrophil count and protein content in Group 2. Group 3, however, showed no significant differences in these parameters compared with control animals. Despite severe neutropenia, lung myeloperoxidase content at 5 h was significantly reduced in Group 3 compared with Group 2. There was no significant difference in pulmonary and systemic hemodynamics between Groups 2 and 3. Group 4 animals exhibited a transient neutropenia, but otherwise no other differences in measured parameters were found compared with Group 1 control animals. In conclusion, EL-246 significantly reduced neutrophil accumulation in lung and attenuated sepsis-induced lung injury, but failed to attenuate deranged pulmonary and systemic hemodynamics.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19950810
Record Date Completed: 19950810

2/7/22 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

126292188 CA: 126(22)292188a JOURNAL
Control of Leishmania major infection in BALB/c mice by inhibition of early lymphocyte entry into peripheral lymph nodes
AUTHOR(S): Laskay, Tamas; Wittmann, Irene; Diefenbach, Andreas; Roellinghoff, Martin; Solbach, Werner
LOCATION: Institute for Clinical Microbiology and Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, D-91054
JOURNAL: J. Immunol. DATE: 1997 VOLUME: 158 NUMBER: 3 PAGES: 1246-1253 CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists
SECTION:
CA215005 Immunochemistry
IDENTIFIERS: Leishmania T lymphocyte L selectin antibody
DESCRIPTORS:
Interferon .gamma.... Leishmania major... Lymph node... L-selectin... Monoclonal antibodies... T cell(lymphocyte)... Th1 cell...
control of Leishmania major infection in BALB/c mice by inhibition of early lymphocyte entry into peripheral lymph nodes with anti-L-selectin monoclonal antibody

2/7/23 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

121155753 CA: 121(13)155753p PATENT
Humanized antibodies to L-selectin
INVENTOR(AUTHOR): Co, Man Sung
LOCATION: USA
ASSIGNEE: Protein Design Labs, Inc.
PATENT: PCT International ; WO 9412215 A1 DATE: 940609
APPLICATION: WO 93US11612 (931130) *US 983946 (921201)
PAGES: 60 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A; C07K-015/28B; C12N-015/13B; C12P-021/08B DESIGNATED COUNTRIES: AT; AU; BB; BG; BR; BY; CA; CH; CZ; DE; DK; ES; FI; GB; HU; JP; KP; KR; KZ; LK; LU; LV; MG; MN; MW; NL; NO; NZ; PL; PT; RO; RU; SD; SE; SK; UA; US; VN
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA215003 Immunochemistry
CA201XXX Pharmacology
IDENTIFIERS: selectin L humanized antibody
DESCRIPTORS:
Gene,animal...
cDNA, for mouse and humanized antibodies to L-selectins, cloning and expression of
Deoxyribonucleic acid sequences,complementary...
for anti-L-selectin antibodies of mouse and humanized
Glycoproteins,specific or class, L-selectins...
humanized antibodies to
Inflammation inhibitors...
humanized antibodies to L-selectins as
Thrombolytics...
humanized antibodies to L-selectins as inflammation inhibitors and, in treatment of ischemia-reperfusion injury
Autoimmune disease... Respiratory distress syndrome,adult... Sepsis and Septicemia...
humanized antibodies to L-selectins as inflammation inhibitors in treatment of
Antibodies... Immunoglobulins,G1... Immunoglobulins,G4...
humanized, to L-selectins
Perfusion,re-...
injury in, prevention of, humanized antibodies to L-selectins as inflammation inhibitors in

Protein sequences...
    of anti-L-selectin antibodies of mouse and humanized
Heart,disease, infarction... Ischemia...
    reperfusion injury in, prevention of, humanized antibodies to
    L-selectins as inflammation inhibitors in
  CAS REGISTRY NUMBERS:
157546-85-5 157546-86-6 157546-87-7 157546-88-8 amino acid sequence of
157546-83-3 157546-84-4 amino acid sequence of, in prepn. humanized
    antibodies
157546-89-9 157546-90-2 nucleotide sequence and expression of
157546-81-1 157546-82-2 nucleotide sequence of, in prepn. humanized
    antibodies
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PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES
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PLEASE LOGON:
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ENTER PASSWORD:
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Welcome to DIALOG

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Last logoff:  28jul99 15:06:48
Logon file001 29jul99 17:19:18
ANNOUNCEMENT    ****    ANNOUNCEMENT    ****    ANNOUNCEMENT
NEW
***Market Guide Company Financials (File 100)
***Frost & Sullivan Market Engineering  (File 767)
***Canada Newswire (File 616 for current news, File 816 for archive)
***So America Bus Info (File 617 for current news, File 817
     for archive news)
***UPI News (Files 261 for current news & 861 for archive news)
***Africa News (Files 606 for current news & 806 for archive news)
***ITAR/TASS (Files 607 for current news & 667 for archive news)
***Xinhua News (Files 618 for current news & 818 for archive news)
***Business Wire (Files 610 for current news & 810 for archive news)
***PR Newswire (Files 613 for current news & 813 for archive news)
***U.S. Newswire (Files 605 for current news & 665 for archive news)
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***Gale Group New Product Announcements (File 621)
***Aerospace/Defense Markets & Technology (File 80)
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***Philosopher's Index (File 57)

     >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
     >>>    of new databases, price changes, etc.      <<<

File   1:ERIC  1966-1999/Jul
       (c) format only 1999 The Dialog Corporation

      Set  Items  Description
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? b 410

>>>'IALOG' not recognized as set or accession number
? set hi ;set hi

       29jul99 17:19:24 User208760 Session D1297.1
            $0.26    0.080 DialUnits File1
     $0.26  Estimated cost File1
            FTSNET   0.016 Hrs.
     $0.26  Estimated cost this search
     $0.26  Estimated total session cost   0.080 DialUnits

File 410:Chronolog(R)  1981-1999 Jul/Aug
       (c) 1999 The Dialog Corporation plc
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? begin begin 55,72,154,399,357

>>>"BEGIN" is not a valid category or service name
       29jul99 17:19:35 User208760 Session D1297.2
            $0.00    0.041 DialUnits File410
     $0.00  Estimated cost File410
            FTSNET   0.002 Hrs.
     $0.00  Estimated cost this search
     $0.26  Estimated total session cost   0.121 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File  55:Biosis Preiviews(R)  1993-1999/Jul W1
        (c) 1999 BIOSIS
*File  55: File is reloaded. Accession number changed.
  File  72:EMBASE  1993-1999/Jul W2
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  File 154:MEDLINE(R)  1993-1999/Sep W4
        (c) format only 1999 Dialog Corporation
*File 154: reloaded, note accession numbers changed.
  File 399:CA SEARCH(R)  1967-1999/UD=13105
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*File 357: Derwent changes DialUnit pricing from May 1, 1999.  See
HELP DERWENT for details.

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? s (l(w)selectin) and (heart(w)lung(w)machine or extracoporeal)

          651062  L
           17080  SELECTIN
            5134  L(W)SELECTIN
          567765  HEART
          324532  LUNG
           20751  MACHINE
             295  HEART(W)LUNG(W)MACHINE
              28  EXTRACOPOREAL
      S1       2  (L(W)SELECTIN) AND (HEART(W)LUNG(W)MACHINE OR
                  EXTRACOPOREAL)
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      S2       2  RD S1 (unique items)
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 2/3/1     (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.

09932982   99230034
  Leukocyte  depletion during cardiac operation: a new approach through the
venous bypass circuit.
  Gu YJ; de Vries AJ; Vos P; Boonstra PW; van Oeveren W
  Department  of Cardiothoracic Surgery, University Hospital Groningen, The
Netherlands.
  Ann   Thorac   Surg (UNITED  STATES)   Mar  1999,  67  (3)  p604-9,  ISSN
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0003-4975 Journal Code: 683
Languages: ENGLISH
Document type: CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL

2/3/2 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08609211 95202670
Neutrophil activation in paediatric extracorporeal circuits: effect of circulation and temperature variation.
el Habbal MH; Carter H; Smith LJ; Elliott MJ; Strobel S
Cardiothoracic Unit, Hospital for Sick Children, London, United Kingdom.
Cardiovasc Res (ENGLAND) Jan 1995, 29 (1) p102-7, ISSN 0008-6363
Journal Code: COR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
? t s2/7/2

2/7/2 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08609211 95202670
Neutrophil activation in paediatric extracorporeal circuits: effect of circulation and temperature variation.
el Habbal MH; Carter H; Smith LJ; Elliott MJ; Strobel S
Cardiothoracic Unit, Hospital for Sick Children, London, United Kingdom.
Cardiovasc Res (ENGLAND) Jan 1995, 29 (1) p102-7, ISSN 0008-6363
Journal Code: COR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
OBJECTIVE: Upregulation of neutrophil adhesion molecules (CD11b and **L-selectin**) and release of a modulating cytokine (IL8) have been reported in vivo and in vitro in adult cardiopulmonary bypass. The aim of this study was to determine whether paediatric bypass preparations have similar influences and whether neutrophil-endothelium interactions are required for IL8 release. METHODS: In vitro paediatric cardiopulmonary bypass circuits (n = 15) were constructed (identical to those used clinically), as well as static loops (n = 15) using donor blood. The effects of circulation and temperature (17 degrees C, 25 degrees C, 37 degrees C) on the initiation of acute inflammation were examined. Cellular expressions of neutrophil adhesion molecules CD11b and **L-selectin** were assayed by immunofluorescence technique, and serum IL8, IL6, TNF-alpha, leucocyte elastase, and terminal complement complex were measured by ELISA. RESULTS: In all experiments, an immediate increase in CD11b expression occurred [median values, in relative fluorescence units: 64.9 (range 45.3-212.9) at rest; 365.2 (205-835.4) at 10 min; $P < 0.001$], along with a decrease in **L-selectin** expression [153.5 (115.5-220.7) at rest; 42 (12-134) at 10 min; $P < 0.01$]. Serum concentrations of the following increased gradually and were higher in circulation than in static loops: IL8 [1500 (500-2500) pg.ml-1 in circuit v 600 (180-1500) pg.ml-1 in loop, $P < 0.001$]; TNF-alpha $P < 0.05$]; and terminal complement complex [25.9 (6.8-120) v 4.7 (0-21.6) AU.ml-1, $P < 0.01$]. Cooling decreased and rewarming increased upregulation of CD11b and downregulation of **L-selectin** and release of IL8. IL6 was undetectable. CONCLUSIONS: In the absence of endothelium, in vitro paediatric cardiopulmonary bypass causes profound acute inflammatory changes in donor blood with release of IL8. These changes were greater than in adult cardiopulmonary bypass. Temperature variation and circulation modulate the responses.
? s L(w)selectin and extracorporeal

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          651062  L
           17080  SELECTIN
            5134  L(W)SELECTIN
           18746  EXTRACORPOREAL
      S3      31  L(W)SELECTIN AND EXTRACORPOREAL
? rd s3

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      S4      20  RD S3 (unique items)
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 4/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:Biosis Preiviews(R)
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11511993   BIOSIS NO.: 199800293325
A CLA-positive and L-selectin-negative cutaneous T-cell
  lymphoma with transition of a skin homing to a lymphnode homing phenotype
  after treatment with extra-corporeal photopheresis (ECP).

AUTHOR: Kleinhans M; Gilliet M; Dummer R; Burg G; Nestle F O
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JOURNAL: Journal of Dermatological Science  16 (SUPPL. 1):pS228 March, 1998

CONFERENCE/MEETING: Third Joint Meeting of the European Society for
Dermatological Research, Japanese Society for Investigative Dermatology,
Society for Investigative Dermatology  Cologne, Germany  May 7-10, 1998
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ISSN: 0923-1811
RECORD TYPE: Citation
LANGUAGE: English


 4/7/2     (Item 2 from file: 55)
DIALOG(R)File  55:Biosis Preiviews(R)
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10789177   BIOSIS NO.: 199799410322
Attenuation of changes in leukocyte surface markers and complement
  activation with heparin-coated cardiopulmonary bypass.

AUTHOR: Moen Oddvar(a); Hogasen Kolbjorn; Fosse Erik; Dregelid Einar;
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JOURNAL: Annals of Thoracic Surgery  63 (1):p105-111 1997
ISSN: 0003-4975
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background. The inflammatory response induced by cardiopulmonary
  bypass can result in severe organ dysfunction in some patients. This
  postperfusion response is caused mainly by contact between blood and the
  foreign surface of the cardiopulmonary bypass equipment and includes
  adhesion of leukocytes to vascular endothelium, which precedes a series
  of events that mediate inflammatory damage to tissues. Methods. Low-risk
  patients accepted for coronary artery bypass grafting were randomized to
  operation with the cardiopulmonary bypass surface either completely
  heparin coated (Duraflo II) or uncoated. There were 12 patients in each
  group. Blood plasma sampled during cardiopulmonary bypass was analyzed
  for complement activation (C3bc and terminal SC5b-9 complement complex)
  and neutrophil activation (lactoferrin and myeloperoxidase). In addition,
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neutrophils, monocytes, and platelets were counted, and the expression of surface markers on the neutrophils and monocytes (complement receptor (CR) 1, CR3, CR4, and **L-selectin**) and on the platelets (P-selectin and CD41) was quantified with flow cytometry. Results. Clinical and surgical results were similar in both groups. In the group with the heparin-coated surface, the formation of the terminal SC5b-9 complement complex was significantly reduced, and the counts of circulating leukocytes and platelets were significantly less reduced initially but were higher at the end of cardiopulmonary bypass compared with baseline. Also, the expression of CR1, CR3, and CR4 was significantly less upregulated and the **L-selectin**, significantly less downregulated on monocytes and neutrophils. Conclusions. We conclude that heparin coating reduces complement activation and attenuates the leukocyte integrin and selectin response that occurs when uncoated circuits are used.

4/7/3 (Item 3 from file: 55)
DIALOG(R)File 55:Biosis Preiviews(R)

10426243 BIOSIS NO.: 199699047388
Neutrophil and cytokine activation with neonatal **extracorporeal** membrane oxygenation.

AUTHOR: Fortenberry James D(a); Bhardwaj Vijay; Niemer Paula; Cornish J Devn; Wright Jean A; Bland Lee
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JOURNAL: Journal of Pediatrics 128 (5 PART 1):p670-678 1996
ISSN: 0022-3476
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objective: To determine whether **extracorporeal** membrane oxygenation (ECMO), like cardiopulmonary bypass, produces systemic inflammatory responses that could potentiate organ injury in infants with respiratory failure. Study design: We evaluated the effects of neonatal ECMO on neutrophil surface adherence proteins, elastase release, and cytokine levels in blood samples from IS patients before and during ECMO, and from banked blood and ECMO circuit blood before cannulation. Neutrophil elastase, tumor necrosis factor alpha, and interleukin types 1-beta, 6, and 8 were measured. Chest radiographs were evaluated by a radiologist using a lung injury score in blinded fashion. Results: Primed ECMO circuit blood, in comparison with patient pre-ECMO blood, demonstrated marked up-regulation of CD11b (mean fluorescence intensity 1660 +- 109 vs 361 +- 81; p lt 0.001 (mean +- SEM)), shedding of **L-selectin** (mean fluorescence intensity 10 +- 2 vs 89 +- 38; p lt 0.01), and elevated elastase levels (349 +- 76 vs 154 ng/ml +- 38; p lt 0.001), consistent with neutrophil activation. During ECMO, neutrophil CD11b levels increased but **L-selectin** was not significantly shed. Concentrations of circulating neutrophil elastase increased significantly during ECMO. Corrected circulating quantities of interleukin-8 also rose significantly, but the responses of tumor necrosis factor alpha and interleukin-1-beta were minimal. Radiographic lung injury scores worsened with the initiation of ECMO (median score: 6 before ECMO vs 11 in first hour of ECMO; p = 0.012), in conjunction with indicators of neutrophil activation. Conclusion: Neonates with respiratory failure have activation of the inflammatory cascade. ECMO incites additional neutrophil and cytokine activation in association with early pulmonary deterioration. Routine leukodepletion of blood for circuit priming to remove activated neutrophils may be beneficial.

4/7/4 (Item 4 from file: 55)
DIALOG(R)File 55:Biosis Preiviews(R)

10182983 BIOSIS NO.: 199698637901
Effect of heparin anticoagulation on neutrophil adhesion molecules and release of IL8: C3 is not essential.

AUTHOR: El Habbal Magdi H(a); Smith Linda; Elliot Martin J; Strobel Stephan
AUTHOR ADDRESS: (a)Cardiothoracic Unit Host Defence Unit, Inst. Child Health Great Ormond St., Hosp. Children NHS T, UK

JOURNAL: Cardiovascular Research 30 (5):p676-681 1995
ISSN: 0008-6363
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objective: To examine the role of heparin in modulating neutrophil activation and release of cytokine. Background: Up-regulation of CD11b, down-regulation of **L-selectin** on neutrophil cell surface and release of IL8 occur in response to **extracorporeal** circulation (ECC) and were proposed to cause leakage of the capillaries in patients. Design: In a series of experiments, we examined the effect of heparin (4 U/ml) comparing it with ethylenediamine tetra-acetate (EDTA, 1.5 mg/ml) and citrate mixture (100 mu-l/ml), heparin dose-response, IL8 (human recombinant IL8) dose-response and protamine (80 mu-g/ml) neutralization of heparin (4 U/ml) using donor blood (total of 38). The role of complement component type 3 (C3) was tested. Neutrophils from a patient with complete C3 deficiency were stimulated by using heparin and cobra venom factor (10 mu-g/ml) and compared with controls (n = 5). CD11b and **L-selectin** expressions were assayed immediately and serially up to 120 min using immune fluorescence and flow cytometry. Serum concentrations of IL8 were determined by using enzyme-linked immunosorbent assay. Results: The medians of up-regulation of CD11b were 540.2 (range 235.2-653.3) for heparin vs. 186.5 (55.7-207.1) for EDTA and 192.5 (69.2-263.8) for citrate mixture, P lt 0.01 The medians of down-regulation of **L-Selectin** were 79 (32-192) for heparin vs. 18.4 (0-188) for EDTA and 36.2 (7.4- 135) for citrate mixture, P lt 0.05. Up-regulation of CD11b, down-regulation of L-s and release of IL8 were inversely related to heparin concentration (r = 0.87, P lt 0.05). Serum concentration of IL8 had a direct relationship to the changes in CD11b and **L-selectin** expression (r - 0.92). Heparin-protamine complex was less stimulant to expression of CD11b and **L-selectin** than heparin or protamine (P lt 0.05). In blood samples from C3-deficient patients, heparin and cobra venom factor caused up-regulation of CD11b and down-regulation of **L-selectin** similar to that of controls (P gt 0.05). Conclusions: Heparin stimulates up-regulation of neutrophil adhesion molecules CD11b, down-regulation of **L-Selectin** and release of IL8. These effects are inversely related to heparin concentration and are independent or C3 activation. IL8 has a direct relationship to activation of neutrophil adhesion molecules. Increasing heparin dosage reduces neutrophil activation and may reduce the morbidity of patients.

4/7/5 (Item 5 from file: 55)
DIALOG(R)File 55:Biosis Preiviews(R)

10104512 BIOSIS NO.: 199698559430
Studies of the effect of Pall leucocyte filters LG6 and AV6 in an in vitro simulated **extracorporeal** circulatory system.

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JOURNAL: Perfusion 10 (5):p291-300 1995
ISSN: 0267-6591
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neutrophil activation is thought to play a major role in the inflammatory response seen in reperfusion injury and similar clinical situations, i.e. **extracorporeal** circulation. Impairment of neutrophil function or reduction of total numbers of neutrophils using a leucocyte filter may be beneficial in reducing the adverse clinical effects. In this study we have investigated the effect of the Pall LG6 and control AV6 filters during simulated in vitro cardiopulmonary bypass (CPB). Various parameters were evaluated including neutrophils, total leucocytes, monocytes, lymphocytes and platelets, expression of antigens on neutrophils using a panel of leucocyte-associated monoclonal antibodies CD13, 14, 15, 45Ro, 67, 11a, 11b and **L selectin**. The effects of leucocyte stimulation with phorbol myristate acetate (PMA) and a leucocyte bolus from a patient with chronic myeloid leukaemia (CML) were also investigated. We have demonstrated that the LG6 significantly reduces leucocytes, in particular neutrophils, with a modest reduction of lymphocytes, platelets and haematocrit, whereas the AV6 had no effect on leukocytes or neutrophils in the test system. In addition the LG6 was associated with a reduction in expression of all leucocyte antigens by approximately 20%; however there was no appreciable alteration of any of the antigens with AV6. Leucocyte stimulation with PMA resulted in a dramatic decrease of all cellular elements and an extra leucocyte load (using CML leucocytes) was not effectively filtered by the LG6 filter.

4/7/6 (Item 6 from file: 55)
DIALOG(R)File 55:Biosis Preiviews(R)

09679875 BIOSIS NO.: 199598134793
Neutrophil activation in paediatric **extracorporeal** circuits: Effect of circulation and temperature variation.

AUTHOR: El Habbal Magdi H(a); Carter Helen; Smith Linda J; Elliott Martin J ; Strobel Stephan
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JOURNAL: Cardiovascular Research 29 (1):p102-107 1995
ISSN: 0008-6363
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objective: Upregulation of neutrophil adhesion molecules (CD11b and **L-selectin**) and release of a modulating cytokine (IL8) have been reported in vivo and in vitro in adult cardiopulmonary bypass. The aim of this study was to determine whether paediatric bypass preparations have similar influences and whether neutrophil-endothelium interactions are required for IL8 release. Methods: In vitro paediatric cardiopulmonary bypass circuits (n = 15) were constructed (identical to those used clinically), as well as static loops (n = 15) using donor blood. The effects of circulation and temperature (17 degree C, 25 degree C, 37 degree C) on the initiation of acute inflammation were examined. Cellular expressions of neutrophil adhesion molecules CD11b and **L-selectin** were assayed by immunofluorescence technique, and serum IL8, IL6, TNF-alpha, leucocyte elastase, and terminal complement complex were measured by ELISA. Results: In all experiments, an immediate increase in CD11b expression occurred (median values, in relative

fluorescence units: 64.9 (range 45.3-212.9) at rest; 365.2 (205-835.4) at 10 min; P lt 0.001),. along with a decrease in **L-selectin** expression (153.5 (115.5-220.7) at rest, 42 (12-134) at 10 min; P lt 0.01). Serum concentrations of the following increased gradually and were higher in circulation than in static loops: IL8 (1500 (500-2500) pg cntdot ml-1 in circuit v 600 (180-1500) pg cntdot ml-1 in loop, P lt 0.001); TNF-alpha (400 (120-1100) v 50 (0-80) pg cntdot ml-1, P lt 0.001); leucocyte elastase (1388 (778-6977) v 833 (175-1800) ng cntdot ml-1, P lt 0.05); and terminal complement complex (25.9 (6.8-120) v 4.7 (0-21.6) AU cntdot ml-1, P lt 0.01). Cooling decreased and rewarming increased upregulation of CD11b and downregulation of **L-selectin** and release of IL8. IL6 was undetectable. Conclusions: In the absence of endothelium, in vitro paediatric cardiopulmonary bypass causes profound acute inflammatory changes in donor blood with release of IL8. These changes were greater than in adult cardiopulmonary bypass. Temperature variation and circulation modulate the responses.

4/7/7 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

07664623 EMBASE No: 1999138168

Safety issues of plateletpheresis: Comparison of the effects of two cell separators on the activation of coagulation, fibrinolysis, and neutrophils and on the formation of neutrophil-platelet aggregates

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Transfusion (TRANSFUSION) (United States) 1999, 39/4 (420-427)

CODEN: TRANA ISSN: 0041-1132
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

BACKGROUND: Although many donors undergo repeated plateletpheresis, data on the consequences of plateletpheresis for the donor's health remain scarce. Thus, the effect of plateletpheresis on the activation of coagulation, fibrinolysis, and neutrophils was investigated. STUDY DESIGN AND METHODS: Part 1: Sixteen healthy men were randomly assigned to undergo plateletpheresis on a cell separator (AMICUS, Fenwal Baxter; or MCS 3p, Haemonetics). The effects of plateletpheresis on plasma levels of prothrombin fragment (Finf 1inf +inf 2), D-dimer, plasmin-plasmin inhibitor (PPI) complexes, and plasminogen activator inhibitor (PAI-1); on the activation of neutrophils (% **L-selectin**+); and on the frequency of platelet-neutrophil aggregates (% CD41+ neutrophils) were compared. Part 2: Ten healthy men received infusions of ACD-A and placebo without apheresis in a randomized, double-blind crossover study to control for the pharmacologic effects of citrate. RESULTS: Part 1: No change in Finf 1inf +inf 2 occurred ($p>0.05$), which indicated that plateletpheresis did not enhance coagulation. Levels of D-dimer, PPI, and PAI-1 decreased over time on the AMICUS ($p<0.001$). Plateletpheresis did not activate neutrophils ($p>0.05$), but it decreased the percentage of CD41+ neutrophils ($p<0.003$). An approximately 80-percent drop in mononuclear cells was observed in the **extracorporeal** circulation of the AMICUS ($p<0.001$ vs. baseline and $p = 0.005$ vs. MCS 3p), and circulating lymphocyte and monocyte counts decreased concomitantly. Part 2: Infusion of ACD-A slightly decreased D-dimer levels ($p<0.05$), and both infusions decreased the circulating lymphocyte counts. CONCLUSION: Plateletpheresis can be regarded as safe with respect to the activation of coagulation or neutrophils. The consequences for the donor's health of the decrease in D-dimer, PPI, and PAI-1 may deserve further investigation.

4/7/8 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

07647860 EMBASE No: 1999120921
Plasma levels of selectins and interleukins in cardiovascular surgery using cardiopulmonary bypass
Sablotzki A.; Dehne M.G.; Mann V.; Gorlach G.; Muhling J.; Zickmann B.; Hempelmann G.
Dr. A. Sablotzki, Anaesthes./Intensive Care Med. Dept., Justus-Liebig-Universitat, Rudolf-Buchheim-Strasse 7, D-35392 Giessen Germany
Thoracic and Cardiovascular Surgeon (THORAC. CARDIOVASC. SURG.) (Germany) 1999, 47/1 (26-31)

CODEN: TVCHA ISSN: 0171-6425
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 24

Background: Cardiovascular surgery with cardiopulmonary bypass (CPB) leads to activation of a variety of inflammatory pathways, including the release of cytokines and selectins. Methods: In 20 patients undergoing elective coronary artery bypass grafting, plasma levels of interleukins IL-2, -6, -8, -10, -12 and of P-, E-, and L-selectins were measured at eight time points before, during, and after CPB using a standardized ELISA technique. Results: IL-2 plasma levels decreased significantly after the start of CPB and remained low until the second postoperative day. IL-6 and IL-8 levels increased significantly after weaning off CPB, with mean peak values six hours postoperatively. Very low IL-10 plasma levels were-detectable preoperatively. They remained low during CPB and peaked significantly after weaning off CPB until skin closure. The IL-12 levels decreased after weaning off CPB ($p<0.05$) until 6 hours postoperatively. The plasma levels of P-selectin showed no alterations, but concentrations of E- and **L-selectin** decreased after the start of CPB ($p<0.05$). There were no adverse postoperative events. Conclusions: The results of our study demonstrate a dysregulation of cytokine and selectin production during and up to 48 h after CPB, which may be a 'normal' stress reaction to CPB.

4/7/9 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE

07069410 EMBASE No: 1997351273
Effect of methylprednisolone on the oxidative burst activity, adhesion molecules and clinical outcome following open heart surgery
Toft P.; Christiansen K.; Tonnesen E.; Nielson C.H.; Lillevang S.
Dr. P. Toft, Dept. Anaesthesiology Intensive Care, University Hospital of Arhus, Arhus Kommunehospital, Norrebrogade 44, DK-8000 Arhus C Denmark
Scandinavian Cardiovascular Journal (SCAND. CARDIOVASC. J.) (Norway) 1997, 31/5 (283-288)

CODEN: SCJOF ISSN: 1401-7431
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 23

Following cardiac surgery with cardiopulmonary bypass (CPB), activated granulocytes may be involved with ischaemia/reperfusion injury. The purpose of this study was to investigate whether steroids could reduce the oxidative burst activity of granulocytes, the expression of adhesion molecules on granulocytes and improve clinical outcome. Sixteen patients undergoing open heart surgery participated in the study. Eight were randomized to receive methylprednisolone (30 mg/kg intravenously) at the

start of anaesthesia while eight patients served as a control group. The oxidative burst was measured flow cytometrically using 123-dihydrorhodamine. A panel of adhesion molecules was measured using monoclonal antibodies. Following CPB the oxidative burst activity and the expression of the adhesion molecule **L-selectin** more than doubled compared to initial values. There was no difference between the steroid group and the control group regarding the expression of adhesion molecules or the oxidative burst activity. In the steroid group the fluid gain during **extracorporeal** circulation (ECC) was 683 ml (median) compared to 1488 ml in the control group. Steroids prevented hyperthermia in the postoperative period but did not improve the weaning from the ventilator or reduce the stay in the intensive-care unit. In conclusion, treatment with steroids prevented hyperthermia following open heart surgery with CPB and reduced capillary leak during ECC. Methylprednisolone, however, did not reduce the oxidative burst activity or the expression of adhesion molecules on granulocytes following CPB.

4/7/10 (Item 4 from file: 72)
DIALOG(R)File 72:EMBASE

05954459 EMBASE No: 1994363324
Neutrophil dynamics and retention in lung, oxygenator, and arterial filter during cardiopulmonary bypass in a pig model

Dewanjee M.K.; Palatianos G.N.; Kapadvanjwala M.; Hsu L.-C.; Novak S.; Balantino G.; Serafini A.N.; Dietrich W.D.; Sfakianakis G.N.
Division of Nuclear Medicine, Miami University School of Medicine, P. O. Box 016960,Miami, FL 33101 United States

ASAIO Journal (ASAIO J.) (United States) 1994, 40/3 (M547-M553)

CODEN: AJOUE ISSN: 1058-2916
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Interactions of neutrophils with adsorbed proteins in components of the cardiopulmonary bypass (CPB) circuit and expression of leukocyte adhesion molecules on activated neutrophils affect neutrophil kinetics and margination. Lung and skeletal muscle along with oxygenator (OX) and arterial filter (AF) in the **extracorporeal** circuit provide the major areas of neutrophil (N) interaction. The dynamics of N-interaction and N-retention during 3 hr CPB was quantified with autologous In-111 labeled neutrophils (INN) in 4 groups of 20 Yorkshire pigs (28-35 kg, 5 sham; 5 CPB, 1 hr; 5 CPB, 3 hr and 5 CPB with heparinized circuit, 3 hr); anesthetized pigs were injected with INN (500-650 muCi), 30 min before CPB and heparinized, and underwent CPB° with a roller pump, a hollow fiber OX (Bentley CM 50, 5.0 msup 2) and AF (Bentley AF 025, 0.25msup 2) at 2.5-3.6 l/min for 3 hr. N-dynamics on OX and AF was monitored by a calibrated Geiger probe. Neutrophil deposition, like that of plasma proteins on OX, reached a steady state almost instantly, but increased on filter with CPB time. INN distribution was viewed with a gamma camera; total INN was measured with an ion chamber and INN in samples of fibers and tissues was quantified with a gamma counter. INN in lung did not change significantly during CPB and increased in liver. The percentage of injected INN in lung, liver, and brain changed with CPB time and showed significant increase over sham-operated animals. Heparin coating of components decreased INN retention. INN/metersup 2 of lung, OX, and AF at 3 hr were 0.26 +/- 0.07%, 0.06 +/- 0.02%, and 6.17 +/- 3.94%, and significantly lower on a heparin coated filter (2.14 +/- 1.30)%. Capillary surface areas of viscera and connective tissues (lung, 100; liver, 134; spleen, 20; heart, 7; skeletal muscle, 92; fat, 12; bone, 3; bone marrow, 5; brain, 0.1 metersup 2) were estimated from distribution of activated INN in pigs. Lung INN retention was much higher than that of the polymer surfaces of OX/AF, indicating the role of cell adhesion molecules on INN retention on endothelial cells of lung and viscera. By direct continuous monitoring and quantitation of INN at the end of CPB, a sensitive technique for quantitation of neutrophil

kinetics, margination, and retention during CPB was developed.

4/7/11 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09285012 97467045
Small-molecule selectin inhibitor protects against liver inflammatory response after ischemia and reperfusion.
Palma-Vargas JM; Toledo-Pereyra L; Dean RE; Harkema JM; Dixon RA; Kogan TP
Surgical Research Institute at Borgess Medical Center, Kalamazoo, MI 49001, USA.
J Am Coll Surg (UNITED STATES) Oct 1997, 185 (4) p365-72, ISSN 1072-7515 Journal Code: BZB
Languages: ENGLISH
Document type: JOURNAL ARTICLE
BACKGROUND: The selectin family of adhesion molecules plays a key role in the neutrophil-mediated injury observed after ischemia and reperfusion. In our study, we investigated the effects of TBC-1269, a novel small-molecule, nonoligosaccharide inhibitor of P-, E-, and **L-selectin** binding, in the liver inflammatory response after 90 minutes of warm ischemia. STUDY DESIGN: Total liver ischemia was produced in Sprague-Dawley rats for 90 minutes using an **extracorporeal** portosystemic shunt. The animals were divided into five groups including: the sham (group 1), ischemic control (group 2) receiving only the vehicle, and the treated groups receiving TBC-1269 at a dose of 25 mg/kg at different times of administration: 15 minutes before reperfusion (group 3), at reperfusion (group 4), and 15 minutes after reperfusion (group 5). The following indices were analyzed: 7-day survival, liver injury tests, liver tissue myeloperoxidase as an index of neutrophil infiltration, and liver histology. RESULTS: TBC-1269 treated groups experienced a significant increase in survival compared with controls. Best overall survival, 70%, was observed when TBC-1269 (Texas Biotechnology Corporation, Houston, TX) was administered 15 minutes before reperfusion ($p < 0.05$). This group also showed a marked decrease ($p < 0.05$) in liver enzyme levels at 6 hours after reperfusion. Neutrophil migration was also significantly ameliorated (81%), as reflected by decreased myeloperoxidase levels. We observed improved histologic damage scores in the treated group compared with controls ($p < 0.05$). CONCLUSIONS: A small-molecule selectin inhibitor (TBC-1269) had a protective effect in livers subjected to 90 minutes of warm hepatic ischemia and 6 hours of reperfusion by decreasing neutrophil infiltration, migration and subsequent tissue damage. The best protective effect was achieved when the compound was administered 15 minutes before reperfusion. These findings offer a new therapeutic alternative for protection against ischemia and reperfusion injury.

4/7/12 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09099474 97278424
Effects of heparin coating on the expression of CD11b, CD11c and CD62L by leucocytes in **extracorporeal** circulation in vitro.
Hogevold HE; Moen O; Fosse E; Venge P; Braten J; Andersson C; Lyberg T
Department of Surgery and Research Forum, Ullev.ANG.al Hospital, University of Oslo, Norway.
Perfusion (ENGLAND) Mar 1997, 12 (1) p9-20, ISSN 0267-6591 Journal Code: BDD
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Leucocyte adhesion molecules are involved in the leucocyte-endothelial interaction and in the activation of coagulation and binding of complement and endotoxin. Thus, they are important in inflammation, systemic acute

phase reaction, ischaemia reperfusion injury and resistance against infections. The expression of the adhesion molecules CD11b, CD11c and CD62L on leucocytes and changes in plasma products of neutrophil activation (myeloperoxidase, lactoferrin) and complement activation (C3bc, SC5b-9 (TCC)) were examined in an **extracorporeal** circulation (ECC) model and the effects of Carmeda bioactive surface (CBAS) heparin coating (n = 7) of the circuits were compared to uncoated control circuits (n = 5). In this model, new 'unactivated' cells mobilized from the bone marrow could not interfere with descriptive measures of cell activation as seen in in vivo studies. In the control group, CD11b and CD11c were upregulated on monocytes and granulocytes during ECC, whereas CD62L was downregulated. Heparin coating reduced the increase in CD11b and CD11c on granulocytes ($p < 0.02$ at 2 h), but the delayed increase in CD11c on monocytes and the delayed downregulation of CD62L on granulocytes and monocytes did not reach statistical significance. Further, heparin coating also reduced the initial decrease in the absolute cell counts of monocytes and granulocytes ($p = 0.01$ at 2 h), reflecting reduced adhesion to the oxygenator/tubing. The increases in plasma myeloperoxidase, lactoferrin, C3bc and TCC were lower in the heparin-coated group compared to the control group. The increases in plasma myeloperoxidase and lactoferrin correlated significantly to the increase in CD11b ($r = 0.71$, $p = 0.02$ and $r = 0.64$, $p = 0.05$, respectively) and CD11c ($r = 0.72$, $p = 0.008$ and $r = 0.72$, $p = 0.008$, respectively) on granulocytes, suggesting interacting regulatory pathways in the process of neutrophil adhesion, activation and degranulation. Thus, in this in vitro ECC model, heparin coating of oxygenator/tubing sets reduced leucocyte activation and leucocyte adhesion-related phenomena.

4/7/13 (Item 3 from file: 154)

08173966 95076970

Effects of aprotinin on complement and granulocyte activation during ex vivo hemodialysis.

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Division of Nephrology, Maine Medical Center, Portland 04102.

Am J Kidney Dis (UNITED STATES) Dec 1994, 24 (6) p901-6, ISSN 0272-6386 Journal Code: 3H5
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Hemodialysis with cellulosic membranes results in complement activation, granulocytopenia, and granulocyte activation. To further investigate the relationship between complement activation and granulocyte activation, we developed a model of ex vivo hemodialysis with blood flow, dialysate flow, and dialysate composition similar to in vivo hemodialysis. We used this model to investigate the effects of aprotinin, a potent serine protease inhibitor frequently used as an anti-inflammatory agent during cardiopulmonary bypass surgery, on both complement and granulocyte activation. Seven normal human volunteers were phlebotomized for ex vivo hemodialysis on two occasions each, one with and once without 800,000 kallikrein inhibitor units of aprotinin added to the circuit. Measurements were made of complement activation (radioimmunoassay for C3a desArg and C5a desArg), as well as granulocyte activation (flow cytometric measurements of reactive oxygen species (ROS) production, granulocyte CD11b-CD18 [MAC-1, CR3] expression, and CD62-L [**L-selectin**] expression).
Statistically significant elevations in C3a desArg levels occurred by 10 minutes and reached a maximum of 5,367 +/- 712 ng/mL by 60 minutes after the initiation of ex vivo hemodialysis. Plasma C5a levels were elevated to 236 +/- 32 ng/mL at 60 minutes compared with 45 +/- 15 ng/mL predialysis. Aprotinin was able to significantly inhibit dialysis-induced C3a generation (peak 2,456 +/- 572 ng/mL at 60 minutes) as well as C5a generation (86 +/- 23 ng/mL at 60 minutes). During ex vivo hemodialysis, there was also a significant increase in granulocyte ROS production, MAC-1 upregulation, and **L-selectin** downregulation. Changes in granulocyte activation were not affected by the administration of aprotinin.(ABSTRACT TRUNCATED AT

250 WORDS)

4/7/14 (Item 4 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

07806141 94091906
Humoral and cellular activation in a simulated **extracorporeal** circuit.
Moat NE; Rebuck N; Shore DF; Evans TW; Finn AH
Royal Brompton National Heart and Lung Hospital, London, England.
Ann Thorac Surg (UNITED STATES) Dec 1993, 56 (6) p1509-14, ISSN 0003-4975 Journal Code: 683
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Endothelial injury consequent upon widespread humoral and cellular activation is probably a major contributor to the phenomenon of cardiopulmonary bypass-induced organ dysfunction. This article reviews some of the mechanisms by which complement and neutrophil activation and interleukin-8 may be involved in this inflammatory response. In a model consisting of a simulated **extracorporeal** circulation we were able to demonstrate complement activation, profound and specific changes in neutrophil adhesion molecule expression, and interleukin-8 generation. The importance of these changes and their potential interactions are discussed.

4/7/15 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

129314486 CA: 129(24)314486n JOURNAL
Clinical and basic studies on the G-1 column, a new extracorporeal therapeutic device effective in controlling rheumatoid arthritis
AUTHOR(S): Kyogoku, M.; Kasukawa, R.
LOCATION: Otsuka Pharmaceutical Co., Ltd., Otsu, Japan, 520
JOURNAL: Inflammation Res. DATE: 1998 VOLUME: 47 NUMBER: Suppl.3
PAGES: S166-S176 CODEN: INREFB ISSN: 1023-3830 LANGUAGE: English
PUBLISHER: Birkhaeuser Verlag
SECTION:
CA214011 Mammalian Pathological Biochemistry
CA263XXX Pharmaceuticals
IDENTIFIERS: G1 blood extracorporeal perfusion rheumatoid arthritis, cellulose acetate blood leukocyte rheumatoid arthritis, rheumatoid marker blood G1 acetate cellulose
DESCRIPTORS:
Proteins(specific proteins and subclasses)...
acidic, acidic sol. serum; inflammation marker removing in extracorporeal blood perfusion by G-1 column in rheumatoid arthritis
Blood proteins...
acidic sol. serum; inflammation marker removing in extracorporeal blood perfusion by G-1 column in rheumatoid arthritis
Adhesive proteins... L-selectin... Mac-1 antigen...
adhesive proteins decrease in extracorporeal blood perfusion by G-1 column in rheumatoid arthritis
Cytokines... Interleukin 1.beta.... Interleukin 6... Interleukin 8... Tumor necrosis factor .alpha....
cytokine suppression in extracorporeal blood perfusion by G-1 column in rheumatoid arthritis
Monocyte... Platelet(blood)... Polymorphonuclear leukocyte...
extracorporeal blood perfusion by G-1 column and granulocyte removing in rheumatoid arthritis
Extracorporeal circulation... Perfusion apparatus... Rheumatoid arthritis ...
G-1 column, extracorporeal blood perfusion device effective in controlling rheumatoid arthritis

CAS REGISTRY NUMBERS:
9002-60-2 biological studies, ACTH increase in extracorporeal blood perfusion by G-1 column in rheumatoid arthritis
50-22-6 corticosterone decrease in extracorporeal blood perfusion by G-1 column in rheumatoid arthritis
60118-07-2 endorphin increase in extracorporeal blood perfusion by G-1 column in rheumatoid arthritis
9004-35-7 G-1 column, extracorporeal blood perfusion device effective in controlling rheumatoid arthritis
80295-42-7 80295-54-1 inflammation marker removing in extracorporeal blood perfusion by G-1 column in rheumatoid arthritis

4/7/16 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128304071 CA: 128(25)304071p PATENT
Method for disrupting cellular adhesion using peptides with a cell adhesion regulatory domain of an adhesion receptor or counter receptor
INVENTOR(AUTHOR): Hawiger, Jack J.; Timmons, Sheila; Liu, Xue-Yan
LOCATION: USA
ASSIGNEE: Vanderbilt University; Hawiger, Jack J.; Timmons, Sheila; Liu, Xue-Yan
PATENT: PCT International ; WO 9816241 A1 DATE: 19980423
APPLICATION: WO 97US18331 (19971009) *US 28420 (19961015)
PAGES: 77 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-038/10A; A61K-038/16B; A61K-031/335B; A61K-031/135B; C07K-007/08B; C07K-014/47B
DESIGNATED COUNTRIES: AU; CA; US
SECTION:
CA201012 Pharmacology
IDENTIFIERS: integrin domain peptide cell adhesion inhibition, receptor adhesion peptide cell adhesion inhibition
DESCRIPTORS:
Receptors...
adhesion receptors and counter receptors; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Fibroblast...
adhesion; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Integrins...
.alpha.; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Integrins...
.alpha.L; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Integrins...
.alpha.M; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Integrins...
.alpha.X; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Integrins...
.beta.; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Tumors(animal)...
cell, adhesion; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Structure-activity relationship...
cell adhesion-inhibiting; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Vascular endothelium...
cell; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Multidrug resistance... P-glycoproteins...

cell-permeable peptide turnover regulation by MDR pump
Signal peptides...
chimeric peptides contg.; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Peptides,biological studies...
fusion peptides; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Export(biological)...
of peptides; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Glycoproteins(specific proteins and subclasses)...
P-cadherin; peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
Adult respiratory distress syndrome... Antiatherosclerotics... Anticoagulants... Antiproliferative agents... Anti-inflammatory drugs... Arterial restenosis... Cadherins... Cardiovascular agents... Cell adhesion molecules... Cell adhesion... Drug transport... Extracorporeal circulation ... E-cadherin... E-selectin... Fibrinogens... ICAM-1(cell adhesion molecule)... ICAM-2(cell adhesion molecule)... ICAM-3(cell adhesion molecule)... Integrin .alpha.IIb... Integrin .beta.1... Integrin .beta.2... Integrin .beta.3... Integrins... Leukocyte... L-selectin... N-cadherin... Peptides,biological studies... Platelet(blood)... Polymorphonuclear leukocyte... Protein sequences... P-selectin... Selectins... Wound healing promoters...
peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
CAS REGISTRY NUMBERS:
206748-57-4D derivs., peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption
52-53-9 79217-60-0 153421-75-1 182752-56-3 206748-53-0 206748-54-1 206748-55-2 206748-56-3 206770-27-6 peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption

4/7/17 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128266260 CA: 128(22)266260q PATENT
Methods using selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
INVENTOR(AUTHOR): Pinsky, David J.; Stern, David; Schmidt, Ann Marie; Rose, Eric A.; Connoly, E. Sander; Solomon, Robert A.; Prestigiacomo, Charles J.
LOCATION: USA
ASSIGNEE: Trustees of Columbia University In the City of New York; Pinsky, David J.; Stern, David; Schmidt, Ann Marie; Rose, Eric A.; Connoly, E. Sander; Solomon, Robert A.; Prestigiacomo, Charles J.
PATENT: PCT International ; WO 9813058 A1 DATE: 19980402
APPLICATION: WO 97US17229 (19970925) *US 721447 (19960927)
PAGES: 230 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-038/00A; A61K-038/02B; A61K-038/17B; A61K-038/36B; A61K-039/395B; C07K-005/00B; C07K-014/00B; C07K-014/435B; C07K-014/745B; C07K-016/00B; C07K-016/18B; C07K-016/28B DESIGNATED COUNTRIES: AU; CA; JP; MX; US
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA201008 Pharmacology
CA214XXX Mammalian Pathological Biochemistry
CA263XXX Pharmaceuticals
IDENTIFIERS: antiischemic stroke selectin antagonist carbon monoxide, inactivated factor IX antiischemic stroke
DESCRIPTORS:
Leukocyte...
accumulation; selectin antagonists, carbon monoxide, and inactivated

factor IX for treating an ischemic disorder and improving stroke outcome

E-selectin... L-selectin... P-selectin... Selectins...
antagonists; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Methemoglobins...
cyanometHbs; Hb spectrophotometric assay to quantify intracerebral hemorrhage

Transient cerebral ischemia...
focal; neutrophil adhesion role in stroke pathogenesis

Cerebral hemorrhage... Spectrophotometry...
Hb spectrophotometric assay to quantify intracerebral hemorrhage

Surgery...
heart; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Surgery...
lung or other; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Transplant(organ)...
lung; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Arterial diseases... Cerebral artery...
middle cerebral artery occlusion; stroke outcome variability after permanent focal cerebral ischemia in relation to mouse strain and other variables

ICAM-1(cell adhesion molecule)... Neutrophil adhesion... Polymorphonuclear leukocyte...
neutrophil adhesion role in stroke pathogenesis

Genes(animal)...
P-selectin; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Organ preservation...
P-selectin-dependent neutrophil adhesion role in hyperthermic/ischemic myocardial preservation

Vascular diseases...
peripheral; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Embolism...
pulmonary; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Nervous system diseases...
reversible ischemic neurol. deficit; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Antithrombotics... Anti-ischemic agents... Extracorporeal circulation... Heart transplant... Inhalants(drug delivery systems)... Intravenous injections... Liver transplant... Lung ischemia... Monocyte... Myocardial infarction... Neutrophil... Oral drug delivery systems... Pancreas transplant... Platelet aggregation inhibitors... Platelet(blood)... Reperfusion injury... Sickle cell anemia... Sprays(drug delivery systems) ... Stroke... Topical drug delivery systems... Transient cerebral ischemia ... Transplant(organ)... Venous thrombosis...
selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome

Drug screening... Focal cerebral ischemia... Reperfusion...
selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome, and anti-ischemic compd. identification method

Carbohydrates,biological studies... Monosaccharides... Nucleic acids... Oligosaccharides,biological studies... Peptidomimetics... Proteins(general),biological studies... Ribozymes...

selectin antagonists; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
Hypothermia... Mouse...
stroke outcome variability after permanent focal cerebral ischemia in relation to mouse strain and other variables
Heart...
surgery; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
Antibodies... Monoclonal antibodies...
to selectins; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
Focal cerebral ischemia...
transient; neutrophil adhesion role in stroke pathogenesis
Lung...
transplant; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
Angina pectoris...
unstable; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
Hypoxia(animal)... Vascular endothelium...
von Willebrand's factor release and P-selectin translocation to cell surface with endothelial cell exposure to hypoxia
Exocytosis...
Weibel-Palade body exocytosis in cardiac surgery
Organelle...
Weibel-Palade body; Weibel-Palade body exocytosis in cardiac surgery
CAS REGISTRY NUMBERS:
10102-43-9 biological studies, agents stimulating; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
630-08-0 biological studies, selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
9001-28-9P inactivated; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
60-92-4 7665-99-8 pathway, agents stimulating; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
37316-87-3 69024-84-6 reaction, in factor IXai prepn.; selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
55-63-0 31356-94-2 33876-97-0 selectin antagonists, carbon monoxide, and inactivated factor IX for treating an ischemic disorder and improving stroke outcome
109319-16-6 von Willebrand's factor release and P-selectin translocation to cell surface with endothelial cell exposure to hypoxia

4/7/18 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127189639 CA: 127(14)189639v JOURNAL
Serum soluble selectins in patients undergoing cardiopulmonary bypass. Relationship with circulating blood cells and inflammation-related cytokines
AUTHOR(S): Diago, M. C.; Garcia-Unzueta, M. T.; Marcano, G.; Merino, J.; Salas, E.; Amado, J. A.
LOCATION: Department of Anaesthesiology, Hospital Universitario Marques de Valdecilla, Cantabria University, Santander, Spain,
JOURNAL: Acta Anaesthesiol. Scand. DATE: 1997 VOLUME: 41 NUMBER: 6
PAGES: 725-730 CODEN: AANEAB ISSN: 0001-5172 LANGUAGE: English

PUBLISHER: Munksgaard
SECTION:
CA215010 Immunochemistry
CA214XXX Mammalian Pathological Biochemistry
CA263XXX Pharmaceuticals
IDENTIFIERS: cardiopulmonary bypass sol selectin blood cell, inflammatory cytokine cardiopulmonary bypass heart surgery
DESCRIPTORS:
Extracorporeal circulation...
cardiopulmonary bypass; serum sol. selectins in patients undergoing cardiopulmonary bypass in relation to circulating blood cells and inflammation-related cytokines
Surgery...
heart; serum sol. selectins in patients undergoing cardiopulmonary bypass in relation to circulating blood cells and inflammation-related cytokines
Cytokines...
proinflammatory; serum sol. selectins in patients undergoing cardiopulmonary bypass in relation to circulating blood cells and inflammation-related cytokines
Interleukin 10... Interleukin 12... Interleukin 6... Interleukin 8...
Leukocyte... Platelet(blood)...
serum sol. selectins in patients undergoing cardiopulmonary bypass in relation to circulating blood cells and inflammation-related cytokines
E-selectin... L-selectin... P-selectin...
sol.; serum sol. selectins in patients undergoing cardiopulmonary bypass in relation to circulating blood cells and inflammation-related cytokines
Heart...
surgery; serum sol. selectins in patients undergoing cardiopulmonary bypass in relation to circulating blood cells and inflammation-related cytokines

4/7/19 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

126263165 CA: 126(20)263165k PATENT
Anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
INVENTOR(AUTHOR): Haselbeck, Anton; Schumacher, Guenther; Co, Man Sung; Martin, Ulrich
LOCATION: USA
ASSIGNEE: Protein Design Labs, Inc.; Boehringer Mannheim Gmbh; Haselbeck, Anton; Schumacher, Guenther; Co, Man Sung; Martin, Ulrich
PATENT: PCT International ; WO 9706822 A1 DATE: 19970227
APPLICATION: WO 96US13152 (19960814) *EP 95112895 (19950817) *EP 95114696 (19950919) *US 578953 (19951227)
PAGES: 52 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A
DESIGNATED COUNTRIES: AL; AM; AU; BB; BG; BR; CA; CN; CU; CZ; EE; FI; GE; HU; IL; IS; JP; KG; KP; KR; LK; LR; LT; LV; MD; MG; MK; MN; MX; NO; NZ; PL; RO; SG; SI; SK; TR; TT; UA; US; UZ; VN; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM
DESIGNATED REGIONAL: KE; LS; MW; SD; SZ; UG; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA215003 Immunochemistry
IDENTIFIERS: monoclonal antibody selectin multiple organ failure
DESCRIPTORS:
DNA sequences... Extracorporeal circulation... E-selectin...
Immunoglobulins... L-selectin... Monoclonal antibodies... Plasma(blood)...
Protein sequences... P-selectin... Selectins... Serum(blood)...
anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Organ(animal)...

failure; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Antibodies...
humanized; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Organ(animal)...
injury, acute; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Diseases(animal)... Organ(animal)...
multiple organ failure; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Injury...
organ, acute; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Diseases(animal)...
organ failure; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Trauma...
poly-; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
CAS REGISTRY NUMBERS:
188763-45-3 188763-47-5 amino acid sequence; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
188763-44-2 188763-46-4 nucleotide sequence; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage

4/7/20 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

126170299 CA: 126(13)170299s JOURNAL
Effects of inhibition of complement activation using recombinant soluble complement receptor 1 on neutrophil CD11b/CD18 and L-selectin expression and release of interleukin-8 and elastase in simulated cardiopulmonary bypass
AUTHOR(S): Finn, Adam; Morgan, B. Paul; Rebuck, Naomi; Klein, Nigel; Rogers, Catherine A.; Hibbs, Martin; Elliott, Martin; Shore, Darryll F.; Evans, Timothy W.; Strobel, Stephan; Moat, Neil
LOCATION: Department of Peidatrics, Children's Hospital Sheffield, UK,
JOURNAL: J. Thorac. Cardiovasc. Surg. DATE: 1996 VOLUME: 111 NUMBER: 2
PAGES: 451-459 CODEN: JTCSAQ ISSN: 0022-5223 LANGUAGE: English
PUBLISHER: Mosby-Year Book
SECTION:
CA215008 Immunochemistry
IDENTIFIERS: cardiopulmonary bypass complement neutrophil interleukin 8
DESCRIPTORS:
Extracorporeal circulation...
cardiopulmonary bypass; effects of complement inhibition using recombinant sol. complement receptor 1 on neutrophil CD11b/CD18 and L-selectin expression and release of interleukin-8 and elastase in si
Complement receptor type 1... Complement... Interleukin 8... L-selectin... Mac-1 antigen... Neutrophil...
effects of complement inhibition using recombinant sol. complement receptor 1 on neutrophil CD11b/CD18 and L-selectin expression and release of interleukin-8 and elastase in simulated cardiopulmonary
CAS REGISTRY NUMBERS:
9004-06-2 80295-42-7 82986-89-8 effects of complement inhibition using recombinant sol. complement receptor 1 on neutrophil CD11b/CD18 and L-selectin expression and release of interleukin-8 and elastase in simulated cardiopulmonary bypass

2/7/2 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08609211 95202670

Neutrophil activation in paediatric extracorporeal circuits: effect of circulation and temperature variation.

el Habbal MH; Carter H; Smith LJ; Elliott MJ; Strobel S
Cardiothoracic Unit, Hospital for Sick Children, London, United Kingdom.

Cardiovasc Res (ENGLAND) Jan 1995, 29 (1) p102-7, ISSN 0008-6363
Journal Code: COR
Languages: ENGLISH
Document type: JOURNAL ARTICLE

OBJECTIVE: Upregulation of neutrophil adhesion molecules (CD11b and **L-selectin**) and release of a modulating cytokine (IL8) have been reported in vivo and in vitro in adult cardiopulmonary bypass. The aim of this study was to determine whether paediatric bypass preparations have similar influences and whether neutrophil-endothelium interactions are required for IL8 release. METHODS: In vitro paediatric cardiopulmonary bypass circuits (n = 15) were constructed (identical to those used clinically), as well as static loops (n = 15) using donor blood. The effects of circulation and temperature (17 degrees C, 25 degrees C, 37 degrees C) on the initiation of acute inflammation were examined. Cellular expressions of neutrophil adhesion molecules CD11b and **L-selectin** were assayed by immunofluorescence technique, and serum IL8, IL6, TNF-alpha, leucocyte elastase, and terminal complement complex were measured by ELISA. RESULTS: In all experiments, an immediate increase in CD11b expression occurred [median values, in relative fluorescence units: 64.9 (range 45.3-212.9) at rest; 365.2 (205-835.4) at 10 min; $P < 0.001$], along with a decrease in **L-selectin** expression [153.5 (115.5-220.7) at rest; 42 (12-134) at 10 min; $P < 0.01$]. Serum concentrations of the following increased gradually and were higher in circulation than in static loops: IL8 [1500 (500-2500) pg.ml-1 in circuit v 600 (180-1500) pg.ml-1 in loop, $P < 0.001$]; TNF-alpha $P < 0.05$]; and terminal complement complex [25.9 (6.8-120) v 4.7 (0-21.6) AU.ml-1, $P < 0.01$]. Cooling decreased and rewarming increased upregulation of CD11b and downregulation of **L-selectin** and release of IL8. IL6 was undetectable. CONCLUSIONS: In the absence of endothelium, in vitro paediatric cardiopulmonary bypass causes profound acute inflammatory changes in donor blood with release of IL8. These changes were greater than in adult cardiopulmonary bypass. Temperature variation and circulation modulate the responses.

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                              ***
RELOADED
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***Book in Print (File 470)
***Kompa Latin America (File 586)

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   OneSearch simply BEGIN FIRST for coverage from Dialog's
   broad spectrum of news wires.

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File   1:ERIC  1966-2000/Feb
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      Set  Items  Description
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? b 410

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? set hi ;set hi

       16apr00 07:02:38 User208760 Session D1522.1
            $0.36    0.103 DialUnits File1
     $0.36  Estimated cost File1
     $0.05  TYMNET
     $0.41  Estimated cost this search
     $0.41  Estimated total session cost   0.103 DialUnits

File 410:Chronolog(R)  1981-2000 Mar/Apr
       (c) 2000 The Dialog Corporation plc

      Set  Items  Description
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?
HILIGHT set on as ''
HILIGHT set on as ''
? begin 5,73,155,399,357

       16apr00 07:02:52 User208760 Session D1522.2
            $0.00    0.049 DialUnits File410
     $0.00  Estimated cost File410
     $0.01  TYMNET
     $0.01  Estimated cost this search
     $0.42  Estimated total session cost   0.152 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2000/Apr W3
         (c) 2000 BIOSIS
  File  73:EMBASE  1974-2000/Mar W3
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*File 73: New drug links added. See Help News73.
File 155:MEDLINE(R) 1966-2000/Jun W2
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*File 155: MEDLINE will be reloaded. Accession numbers will change.
File 399:CA SEARCH(R) 1967-2000/UD=13216
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*File 399: Use is subject to the terms of your user/customer agreement.
RANK charge added; see HELP RATES 399.
File 357:Derwent Biotechnology Abs 1982-2000/Apr B2
(c) 2000 Derwent Publ Ltd

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      Set  Items  Description
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? s L(w)selectin and polytrauma?

         1550662  L
           20074  SELECTIN
            5988  L(W)SELECTIN
            3313  POLYTRAUMA?
      S1       0  L(W)SELECTIN AND POLYTRAUMA?
? s polytrauma

      S2    1717  POLYTRAUMA
? s s2 and selectin?

            1717  S2
           58449  SELECTIN?
      S3       7  S2 AND SELECTIN?
? rd s3

...completed examining records
      S4       5  RD S3 (unique items)
? t s4/7/all


 4/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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11022320   BIOSIS NO.: 199799643465
The expression of P-selectin in inflammatory and non-inflammatory
  lung tissue.
AUTHOR: Ortmann C(a); Brinkmann B
AUTHOR ADDRESS: (a)Inst. Rechtsmed., Westfaelische Wilhelms-Univ. Muenster,
  von-Esmarch-Str. 86, D-48149 Muenster**Germany
JOURNAL: International Journal of Legal Medicine  110 (3):p155-158 1997
ISSN: 0937-9827
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: An initial attachment of leukocytes to blood vessel walls is
  mediated by selectins. A feature of adhesion mediated by P-
  selectin is the "rolling" of leukocytes on the endothelium. The
  time dependent expression of p-selectin in lung tissue was
  investigated in five groups of cases with different causes of death:
  carbon-monoxide and cyanide intoxication (n = 11), drowning (n = 5),
  hanging (n = 9), pneumonia (n = 13) and polytrauma with blunt
  thorax trauma (n = 14). In paraffin-embedded archival specimens
  immunostaining was achieved using an adapted APAAP-immunoperoxidase
  technique together with a wet autoclave method. P-selectin
  detection was scored by a semiquantitative method evaluating the
  intensity and incidence of positively stained endothelial cells. The
  distribution pattern of endothelial P-selectin of blood vessels in
  cases of pneumonia and septic shock were heterogenius and weak. In one
  case with lung contusion (survival time 3 h) moderate infiltrates of
```

granulocytes were found near to septal and subpleural hemorrhages. In these inflammatory areas the positive endothelial immunostaining of small vessels was often weaker than in other lung segments or compared to the intensely stained platelets in corresponding vessels.

4/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10558726 BIOSIS NO.: 199699179871
External fixator in the treatment of war bone fractures.
AUTHOR: Stajner Vvan Ante Petricevic(a)
AUTHOR ADDRESS: (a)Dep. Surg., Split Univ. Hosp., Spinciceva 1, 21000 Split **Croatia
JOURNAL: Croatian Medical Journal 37 (3):p165-168 1996
ISSN: 0353-9504
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Aim: Analysis of the course of bone repair in bone fractures caused by high-velocity projectiles in 557 patients. Method: External fixation, a combination of external fixation and minimal internal osteosynthesis, and delayed internal osteosynthesis were used in the treatment of fractures. Primary osteosynthesis was indicated only exceptionally. The choice of the method depended on the type and severity of soft tissue damage, according to a three-grade classification. Results: Most complications requiring reoperation occurred in fractures managed by external fixation alone. There was no lethal outcome either in patients with isolated bone fractures or in those with war **polytrauma** with a predominant extremity bone fracture. Conclusion: Proper stabilization of fractures is of utmost importance for the normal course of fracture healing. A selective approach should therefore be adopted in **selecting** the proper method of treatment for war bone fracture. Division of the wounded into three groups proved very helpful.

4/7/3 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

06594308 EMBASE No: 1996258973
External fixator in the treatment of war bone fractures
Stajner I.; Petricevic A.
Department of Surgery, Split University Hospital, Spinciceva 1,21000 Split Croatia
Croatian Medical Journal (CROAT. MED. J.) (Croatia) 1996, 37/3 (165-168)
CODEN: CMEJE ISSN: 0353-9504
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Aim. Analysis of the course of bone repair in bone fractures caused by high-velocity projectiles in 557 patients. Method. External fixation, a combination of external fixation and minimal internal osteosynthesis, and delayed internal osteosynthesis were used in the treatment of fractures. Primary osteosynthesis was indicated only exceptionally. The choice of the method depended on the type and severity of soft tissue damage, according to a three-grade classification. Results. Most complications requiring reoperation occurred in fractures managed by external fixation alone. There was no lethal outcome either in patients with isolated bone fractures or in those with war **polytrauma** with a predominant extremity bone fracture. Conclusion. Proper stabilization of fractures is of utmost importance for the normal course of fracture healing. A selective approach should therefore be adopted in **selecting** the proper method of treatment for

war bone fracture. Division of the wounded into three groups proved very helpful.

4/7/4 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10174906 20006558
Increase of soluble cytoadhesive molecules sE-**selectin** and sICAM-1 and hyperfibrinogenaemia in patients with **polytrauma** without septicaemia.
Kvasnicka J; Briza J; Krska Z; Kudrna K; Peskova M; Pecen L
Department of Clinical Haematology, General University Hospital, Prague, Czech Republic. kvasnic@okhvfn.anet.cz
Sb Lek (CZECH REPUBLIC) 1998, 99 (2) p93-6, ISSN 0036-5327
Journal Code: UAW
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Multiple organ failure with thrombophilia is suggested to occur in the course of **polytrauma** with septicaemia. The aim of the study was to investigate fibrinogen level, other proteins of acute phase response: positive-orosomucoid and negative-transferrin and soluble cytoadhesive molecules in plasma of patients (n = 28) with **polytrauma** (I-II. stage according to Hannover score) without detectable bacteraemia until 36 hours post injury. The patients treated by massive blood transfusion were excluded. An increase of fibrinogen (Fbg pts 4.34 +/- 2.5 g/l versus control 2.55 +/- 0.55 g/l, p < 0.01), orosomucoid (ORM pts 1.47 +/- 0.8 g/l versus control 0.54 +/- 0.18 g/l, p < 0.01), SE-**selectin** (sE-sel. pts 92.11 +/- 79.4 g/l versus control 46.6 +/- 29.6 g/l, p < 0.05), sICAM-1 (sICAM pts. 698.3 +/- 54.4 versus control 255.6 +/- 58.0 g/l, p < 0.01) and a decrease of transferrin (Trf pts. 1.77 +/- 0.82 versus control 2.83 +/- 0.71 g/l, p < 0.01) were observed in this patients with **polytrauma**. We suppose that an increase of fibrinogen and cytoadhesive molecules sE-**selectin** and sICAM-1 may be induced in patients with **polytrauma** due to a "non-septic" inflammatory acute phase response in the course of wound healing process after tissue injury too.

4/7/5 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120052024 CA: 120(5)52024b JOURNAL
Endothelial and leukocyte activation in experimental polytrauma and sepsis
AUTHOR(S): Redl, H.; Nikolai, A.; Kneidinger, R.; Schlag, G.
LOCATION: Ludwig-Boltzmann Inst. Exp. Clin. Traumatol., A-1200, Vienna, Austria
JOURNAL: Behring Inst. Mitt. DATE: 1993 VOLUME: 92 NUMBER: Vascular Endothelium in Inflammation PAGES: 218-28 CODEN: BHIMA2 ISSN: 0301-0457
LANGUAGE: English
SECTION:
CA215000 Immunochemistry
IDENTIFIERS: leukocyte endothelium polytrauma cytokine review, sepsis leukocyte endothelium cytokine review
DESCRIPTORS:
Injury,trauma... Sepsis and Septicemia...
cytokines and LPS activation of leukocytes and vascular endothelium in relation to
Glycophosphoproteins,E-selectins...
in sepsis, leukocyte and vascular endothelium activation in relation to
Blood vessel,endothelium...
leukocytes and, LPS and cytokines activation of, polytrauma and sepsis in relation to
Lipopolysaccharides...

leukocytes and vascular endothelium activation by, polytrauma and sepsis in relation to
Lymphokines and Cytokines...
proinflammatory, in leukocyte and vascular endothelium activation, polytrauma and sepsis in relation to
Leukocyte... Leukocyte,polymorphonuclear...
vascular endothelium and, LPS and cytokines activation of, polytrauma and sepsis in relation to

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? s l(w)selectin and multiple(w)organ

         1550662  L
           20074  SELECTIN
            5988  L(W)SELECTIN
          824969  MULTIPLE
          376724  ORGAN
           13309  MULTIPLE(W)ORGAN
      S5      23  L(W)SELECTIN AND MULTIPLE(W)ORGAN
? rd s5

...completed examining records
      S6      13  RD S5 (unique items)
? t s6/7/all


 6/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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12324124   BIOSIS NO.: 200000077626
```

L-selectin in trauma patients: A marker for organ dysfunction and outcome?

AUTHOR: Kerner T(a); Ahlers O; Spielmann S; Keh D; Buehrer C; Gerlach M; Hoefler S; Gerlach H
AUTHOR ADDRESS: (a)Abteilung fuer Anaesthesiologie und Operative Intensivmedizin, Charite-Campus Virchow-Klinikum, Augustenburger Platz 1, 13353, Berlin**Germany

JOURNAL: European Journal of Clinical Investigation 29 (12):p1077-1086 Dec., 1999
ISSN: 0014-2972
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Background: Systemic inflammatory response syndrome (SIRS) and **multiple organ** dysfunction syndrome (MODS) are important factors affecting morbidity and mortality after trauma. Adhesion molecules, e.g. **L-selectin** (CD62 L), play crucial roles in both conditions. Patients and methods: In 51 multiple trauma patients, CD62 L surface expression on granulocytes, monocytes, lymphocytes, as well as sCD62 L plasma concentrations were determined during the first 6 days after trauma, starting at the site of accident. Clinical parameters were severity of injury scores (ISS, APACHE II), requirement of red blood cell transfusion, acute lung or liver failure, development of MODS or SIRS, early (ltoreq 6 d) or late (> 6 d), and outcome. Results: CD62 L expression was reversibly elevated on granulocytes, T cells and monocytes in comparison with initial values. sCD62 L plasma concentrations did not show temporal variations but were depressed throughout observation period, in comparison with healthy controls. Lung failure within the first 6 days was associated with increased CD62 L expression on monocytes and B cells on admission and increased sCD62 L concentrations after 12 and 24 h. Patients with more severe injuries (APACHE II>20 points) had higher sCD62 L concentrations after 24 h. Non-survivors had decreased sCD62 L (on admission) and T-cell CD62 L expression (after 4 h). Patients with early MODS or SIRS showed increased monocyte CD62 L expression after 6 days. Conclusions: In multiple trauma patients, severe organ

dysfunction is associated with altered CD62 L expression on leukocytes and circulating sCD62 L plasma concentrations. However, the obvious complexity of the pattern currently restricts use of CD62 L quantitation for clinical purposes.

6/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11610841 BIOSIS NO.: 199800392606
Leukocyte **L-selectin** is up-regulated after mechanical trauma in adults.
AUTHOR: Cocks Robert A(a); Chan Tina Y F; Rainer Timothy H
AUTHOR ADDRESS: (a)Accident Emergency Med. Acad. Unit, Chinese Univ. Hong Kong, Rooms G05/06, Cancer Centre, Prince**Hong Kong
JOURNAL: Journal of Trauma Injury Infection and Critical Care 45 (1):p1-6 July, 1998
ISSN: 1079-6061
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: Infection and **multiple organ** failure remain the principal causes of late mortality after trauma despite advances in the resuscitation of injured patients. Because a better understanding of postinjury leukocyte trafficking is essential to the development of possible therapeutic measures aimed at preventing these complications, we have performed a study of one factor in the early posttrauma endothelial adhesion behavior of monocytes, lymphocytes, and neutrophils: their cell surface expression of **L-selectin** (CD62L). We have also studied the plasma levels of soluble **L-selectin** in these patients. Methods: Two venous blood samples were taken from each of 41 trauma patients at median times of 1 and 20 hours after injury. The study group included 16 patients with major (Injury Severity Score (ISS) gtoreq 16), 17 with moderate (ISS = 9-15), and 8 with minor (ISS < 9) trauma. Cell surface **L-selectin** was measured on leukocyte subsets by staining with specific fluorescent-labeled monoclonal antibodies to CD62L and using flow cytometry. Both the percentage of cells expressing the molecule and the mean channel fluorescence were measured. Levels of soluble **L-selectin** were measured in the plasma, sampled concurrently, by enzyme-linked immunosorbent assay. Results: Monocytes, lymphocytes, and neutrophils all showed an early increase in cell surface **L-selectin** expression as measured by mean channel fluorescence ($p < 0.0001$, $p < 0.001$, and $p < 0.0001$, respectively), and this persisted in later samples taken at a median 20 hours after injury ($p < 0.0001$, $p < 0.0001$, and $p < 0.01$). Only monocytes showed an increased percentage of cells expressing the molecule in the early phase ($p < 0.02$), and this remained in the later phase ($p < 0.001$). Monocytes also showed a further significant increase in mean channel fluorescence ($p < 0.02$) between the two periods. No significant changes in levels of plasma soluble **L-selectin** were found at either stage. Conclusion: An increase in the expression of **L-selectin** on each of three leukocyte populations has been demonstrated in the early phase after trauma. This would tend to promote rolling behavior of leukocytes and increase their contact with the vascular endothelium. There were marked differences in the later responses of the three populations, which may represent differential control of their behavior.

6/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11450861 BIOSIS NO.: 199800232193

Effects of trauma and sepsis on soluble **L-selectin** and cell surface expression of **L-selectin** and CD11b.
AUTHOR: Maekawa K(a); Futami S; Nishida M; Terada T; Inagawa H; Suzuki S; Ono K
AUTHOR ADDRESS: (a)Dep. Traumatol. and Critical Care, Fac. Med., Univ. Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-003**Japan
JOURNAL: Journal of Trauma, Injury, Infection, and Critical Care 44 (3):p 460-468 March, 1998
ISSN: 0022-5282
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objectives: To examine (1) the effects of trauma on changes in neutrophil **L-selectin** and CD11b expression and on the levels of soluble **L-selectin** and (2) whether these alterations are different on leukocyte subpopulations in those patients who develop **multiple organ** dysfunction syndrome. Materials and Methods: Twenty patients with Injury Severity Score (ISS) gtoreq 16 and 15 patients with ISS score < 16 were studied. Arterial blood were collected serially after injury. The staining of leukocyte surface adhesion molecules was performed with antibodies against **L-selectin** and CD11b. Positive cell count and mean fluorescence intensity were determined by flow cytometry. Soluble **L-selectin** was measured using enzyme-linked immunosorbent assay. Results: In patients with ISS gtoreq 16, neutrophil **L-selectin** expression showed an immediate increase, reaching peak levels between 3 to 4 hours after injury ($p < 0.05$ vs. patients with ISS < 16), followed by a gradual decrease. Plasma levels of soluble **L-selectin** reached peak levels at 6 hours after injury. However, in patients with ISS < 16, minimal changes in **L-selectin** expression and soluble **L-selectin** were observed. Neutrophil CD11b expression showed an immediate increase for the first 3 hours followed by a gradual increase up to 24 hours after injury. In patients who developed **multiple organ** dysfunction syndrome, CD11b both on neutrophils and lymphocytes remained elevated for 120 hours. Conclusions: These findings suggest that acute neutrophil activation is an early event after trauma and may be implicated as "a vulnerable window" for leukocyte-mediated end organ injury.

6/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10975320 BIOSIS NO.: 199799596465
Expression of beta-2-integrins and **L-selectin** on polymorphonuclear leukocytes in septic patients.
AUTHOR: Thiel M(a); Zourelidis C; Chambers J D; Von Andrian U H; Arfors K E ; Messmer K; Peter K
AUTHOR ADDRESS: (a)Dep. Anaesthesiol., Klinikum Grosshadern, Marchioninistr. 15, D-81377 Munich**Germany
JOURNAL: European Surgical Research 29 (3):p160-175 1997
ISSN: 0014-312X
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Adhesion molecules on polymorphonuclear leukocytes (PMNL) play an important role in nonspecific defense mechanisms directed at invading microorganisms. When local infection, however, cannot be controlled, a systemic inflammatory response syndrome (SIRS) ensues which may progress to septic shock and **multiple organ** failure, these being major determinants of the patient's outcome. In the present study, the expression of beta-2-integrins and **L-selectin** on blood PMNL was measured on subsequent days in patients with sepsis (n = 17) and in healthy volunteers (n = 15). beta-2-Integrins and **L-selectin**

molecules were detected by flow cytometry, using the monoclonal antibodies IB4 (anti-CD18) and Dreg200 (antiCD62L), respectively. Adhesion molecules were determined at baseline immediately after blood collection and also 45 min after incubation of cells in vitro at body temperature to allow for spontaneous regulation. In addition, PMNL were activated by receptor-dependent and receptor-independent stimuli to characterize stimulus-specific adhesion molecule expression. In parallel with the measurement of adhesion molecules, severity of sepsis was assessed by the Elebute score. The results demonstrate significant differences in the basal, spontaneous and stimulus-induced expression of adhesion molecules between healthy volunteers, survivors (n = 11) and nonsurvivors (n = 6). Moreover, when survivors and nonsurvivors with severe sepsis (Elebute score gt 12) were compared, basal expressions of both beta-2-integrins and **L-selectin** were significantly lower in patients who did not survive. Thus, measurement of adhesion molecules on circulating PMNL may be useful to identify septic patients at high risk for lethal outcome.

6/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09989630 BIOSIS NO.: 199598444548
L-selectin and beta-integrin expression in the systemic inflammatory response syndrome (SIRS).
AUTHOR: Ahmed N A; Giannias B; Christou N V
AUTHOR ADDRESS: Dep. Surg., Royal Victoria Hosp., McGill Univ., Montreal, PQ**Canada
JOURNAL: Clinical and Investigative Medicine 18 (4 SUPPL.):pB25 1995
CONFERENCE/MEETING: Annual Meeting of the Canadian Society for Clinical Investigation and the Royal College of Physicians and Surgeons of Canada Montreal, Quebec, Canada September 13-17, 1995
ISSN: 0147-958X
RECORD TYPE: Citation
LANGUAGE: English

6/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09922011 BIOSIS NO.: 199598376929
Leukocyte activation in the peripheral blood of patients with cirrhosis of the liver and SIRS: Correlation with serum interleukin-6 levels and organ dysfunction.
AUTHOR: Rosenbloom Alan J(a); Pinsky Michael R; Bryant John J; Shin Angela; Tran Thuy; Whiteside Theresa
AUTHOR ADDRESS: (a)Dep. Anesthesiol., Div. Critical Care Med., Univ. Pittsburgh Med. Cent., 200 Lothrop St., Pittsb**USA
JOURNAL: JAMA (Journal of the American Medical Association) 274 (1):p58-65 1995
ISSN: 0098-7484
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objective: Leukocyte adhesion plays an important role in inflammation. Adhesion molecules such as CD11b on polymorphonuclear neutrophil leukocytes (PMNs) up-regulate in response to tumor necrosis factor-alpha, interleukin-8 (IL-8), and other mediators that are involved in systemic inflammatory response syndrome (SIRS). This study examined the behavior of CD11b and other membrane molecules in SIRS in relation to serum cytokines and the severity of illness. Design: Survey study. Setting: Liver transplantation intensive care unit at a tertiary care center. Patients: A consecutive sample of 22 patients admitted to the

liver transplantation intensive care unit for complications related to cirrhosis of the liver in the absence of other disease. Sixteen of the patients developed SIRS and **multiple organ** dysfunction syndrome with suspected bacterial infections. Seven control subjects were also studied. Main Outcome Measures: Modified Goris organ failure score and Acute Physiology and Chronic Health Evaluation II score. Results: Mean serum IL-6 levels, but not IL-1-beta or tumor necrosis factor-alpha levels, correlated with organ failure (r = 0.79, P lt .001). Leukocyte cell-surface markers fluctuated from day to day. The mean of several values was more stable. Mean CD11b and CD35 on PMNs correlated with serum IL-6 level (r = 0.75, P lt .001, and r = 0.77, P lt .005, respectively). Up-regulation of both CD11b and CD35 display on PMNs correlated with organ failure (r = 0.74, P lt .001, and r = 0.71, P lt .01, respectively). Polymorphonuclear neutrophil leukocyte **L-selectin**, CD31, and CD16 were simultaneously decreased, consistent with PMN activation. Monocytes appeared to be activated, but the pattern of surface molecule display was different. Conclusions: In human SIRS, the circulating monocyte and PMN pools undergo alterations suggestive of leukocyte activation, including up-regulation of PMN CD11b in correlation with the serum IL-6 level and severity of organ dysfunction.

6/7/7 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10553671 EMBASE No: 2000018825
Circulating intercellular adhesion molecule-1 as an early predictor of hepatic failure in patients with septic shock
Weigand M.A.; Schmidt H.; Pourmahmoud M.; Zhao Q.; Martin E.; Bardenheuer H.J.
Dr. M.A. Weigand, Department of Anesthesiology, University of Heidelberg, Heidelberg Germany
Critical Care Medicine (CRIT. CARE MED.) (United States) 1999, 27/12 (2656-2661)
CODEN: CCMDC ISSN: 0090-3493
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 28

Objective: To investigate whether endotoxin, interleukin-6, and circulating adhesion molecules, measured sequentially in blood, can predict mortality and organ dysfunction in sepsis. Design: Inception cohort study with follow-up for 28 days. Setting: Surgical intensive care unit at a university hospital. Patients: A total of 14 consecutive patients were enrolled in the study within the first 24 hrs after onset of septic shock. Seven healthy subjects were studied as controls. Interventions: Patients were analyzed for mortality and development of organ dysfunction. Measurements and Main Results: At the end of the 28-day follow-up period, seven of the patients were still alive (survivors) but the other seven (nonsurvivors) had died. At the time of enrollment in the study (day 0), the Acute Physiology and Chronic Health Evaluation II score was 28.4 in survivors (n = 7) and 28.7 in nonsurvivors (n = 7). In contrast, circulating intercellular adhesion molecule-1 (ICAM-1) was significantly higher in non-survivors than in survivors. Circulating ICAM-1 predicted mortality in patients with septic shock with a sensitivity and a specificity of 71.4% each. Endotoxin, interleukin-6, circulating **L-selectin**, P-selectin, E-selectin, and platelet endothelial cell adhesion molecule-1, however, did not distinguish between survivors and nonsurvivors. In addition, circulating ICAM-1 at day 0 showed a significant correlation with the highest serum bilirubin observed during the entire study period (rsup 2 = 0.963). Conclusions: Because only circulating ICAM-1 was higher in nonsurvivors than in survivors at day 0, circulating ICAM-1 may serve as an early prognostic marker for outcome in septic shock. In addition, measurement of circulating ICAM-1 facilitates identification of those patients with the highest risk of developing liver dysfunction.

6/7/8 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

06856617 EMBASE No: 1997139252
Expression of betainf 2-integrins and **L-selectin** on polymorphonuclear leukocytes in septic patients
Thiel M.; Zourelidis C.; Chambers J.D.; Von Andrian U.H.; Arfors K.E.; Messmer K.; Peter K.
Dr. M. Thiel, Department of Anaesthesiology, Klinikum Grosshadern, Marchioninistrasse 15, D-81377 Munich Germany
European Surgical Research (EUR. SURG. RES.) (Switzerland) 1997, 29/3 (160-175)
CODEN: EUSRB ISSN: 0014-312X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 38

Adhesion molecules on polymorphonuclear leukocytes (PMNL) play an important role in nonspecific defense mechanisms directed at invading microorganisms. When local infection, however, cannot be controlled, a systemic inflammatory response syndrome (SIRS) ensues which may progress to septic shock and **multiple organ** failure, these being major determinants of the patient's outcome. In the present study, the expression of betainf 2-integrins and **L-selectin** on blood PMNL was measured on subsequent days in patients with sepsis (n = 17) and in healthy volunteers (n = 15). betainf 2-Integrins and **L-selectin** molecules were detected by flow cytometry, using the monoclonal antibodies IB4 (anti-CD18) and Dreg200 (anti-CD62L), respectively. Adhesion molecules were determined at baseline immediately after blood collection and also 45 min after incubation of cells in vitro at body temperature to allow for spontaneous regulation. In addition, PMNL were activated by receptor-dependent and receptor-independent stimuli to characterize stimulus-specific adhesion molecule expression. In parallel with the measurement of adhesion molecules, severity of sepsis was assessed by the Elebute score. The results demonstrate significant differences in the basal, spontaneous and stimulus-induced expression of adhesion molecules between healthy volunteers, survivors (n = 11) and nonsurvivors (n = 6). Moreover, when survivors and nonsurvivors with severe sepsis (Elebute score > 12) were compared, basal expressions of both betainf 2-integrins and **L-selectin** were significantly lower in patients who did not survive. Thus, measurement of adhesion molecules on circulating PMNL may be useful to identify septic patients at high risk for lethal outcome.

6/7/9 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

05502458 EMBASE No: 1993270557
Leukocytes and the inflammatory response
Mariscalco M.M.
Texas Children's Hospital, MC 2-3450, 6621 Fannin,Houston, TX 77030 United States
Critical Care Medicine (CRIT. CARE MED.) (United States) 1993, 21/9 SUPPL. (S347-S348)
CODEN: CCMDC ISSN: 0090-3493
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH

6/7/10 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09518911 98224922

Pentoxifylline decreases the incidence of **multiple organ** failure in patients after major cardio-thoracic surgery.

Hoffmann H; Markewitz A; Kreuzer E; Reichert K; Jochum M; Faist E

Department of Surgery, Klinikum Grosshadern, Ludwig Maximilians Universitat, Munchen, Germany.

Shock (UNITED STATES) Apr 1998, 9 (4) p235-40, ISSN 1073-2322 Journal Code: CAE

Languages: ENGLISH

Document type: CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL

We assessed the safety and efficacy of intravenous pentoxifylline [3,7-dimethyl-1-(5-oxohexyl)-xanthine] in patients at risk for developing **multiple organ** failure after major cardio-thoracic surgery in a single-center, randomized, placebo-controlled study. Of 816 consecutive patients who underwent major cardio-thoracic surgery, 40 who had Acute Physiology and Chronic Health Evaluation II score values > or = 19 at the first postoperative day after the surgery were included. Patients were randomized to receive either placebo (control; n = 25) or intravenous pentoxifylline treatment (pentoxifylline; n = 15) at a dosage of 1.5 mg/kg/h as an adjunct to standard supportive therapy. Main outcome measurements were duration of required ventilator support, intensive care unit stay, and incidence of renal failure. Thirty-seven patients were eligible for evaluation. No significant adverse events related to pentoxifylline treatment were observed. The duration of mechanical ventilation was significantly greater for control patients (8.3 +/- 3.1 days) compared with pentoxifylline-treated patients (3.1 +/- .9 days; p < .05). Patients treated with pentoxifylline experienced fewer days on hemofiltration (1.2 +/- .8 vs. 6.8 +/- 3.3; p < .05) and a shorter intensive care unit stay (5.2 +/- 1.1 vs. 11.4 +/- 3.1 days). There were no intergroup differences in mortality. Mortality was 33% in the pentoxifylline group and 36% among control group patients. In conclusion, supplemental pentoxifylline treatment may decrease the incidence of **multiple organ** failure in patients at risk of systemic inflammatory response syndrome after cardiac surgery. Additional studies are required to determine the validity of the observed effects.

6/7/11 (Item 2 from file: 155)

09403281 98106907

Alteration in leukocyte adhesion molecule expression following minor, moderate and major trauma.

Cocks RA; Chan TY

Accident and Emergency Medicine Academic Unit, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong.

Eur J Emerg Med (ENGLAND) Dec 1997, 4 (4) p193-5, ISSN 0969-9546 Journal Code: CL2

Languages: ENGLISH

Document type: JOURNAL ARTICLE

An understanding of the mechanisms of post-injury leukocyte trafficking is essential to the development of future therapeutic interventions aimed at preventing infection and **multiple organ** failure in trauma patients, yet very little is known about the cellular and molecular events resulting in mobilization of members of the leukocyte family following trauma. We have studied the post-injury expression of the lymphocyte, monocyte and neutrophil adhesion molecules CD11a (LFA-1), CD11b, CD11c, CD29 (beta-1 integrin) and CD62L (**L-selectin**) in a group of 36 trauma patients, 13 of whom had suffered major trauma (ISS > or = 16), 15 moderate trauma (ISS = 9-15) and eight minor trauma (ISS < 9). Three ml blood samples were taken within 2.5 h of injury (mean sample time = 1.2 h, median = 1 h) into EDTA anticoagulant. Fifty-three normal control subjects were also studied for comparison. Leukocytes were stained using

fluorescent-labelled monoclonal antibodies specific for each adhesion molecule, and the mean receptor density per cell measured using flow cytometry. Monocytes, neutrophils and lymphocytes in the trauma patients showed significantly increased mean-receptor density of **L-selectin** ($p < 0.0001$, 0.0001 and 0.004 respectively). Neutrophils and monocytes showed a significantly decreased level of expression of CD11a, and neutrophils showed a significant decrease in expression of CD11c. Our results indicate that there is a reduction in CD11a expression after trauma which may play an important role in the demargination of neutrophils and monocytes. The strong increase in **L-selectin** expression in all cell populations was unexpected, and is potentially important because this molecule supports rolling behaviour in all members of the leukocyte family, and would promote close contact between leukocytes and the endothelium at the site of injury without firm adhesion taking place. These events may be of significance in planning future strategies to combat post-trauma complications.

6/7/12 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09150863 97345151
Neutrophil adhesion molecules and MOF [editorial; comment]
van Deventer SJ; Pajkrt D
Intensive Care Med (UNITED STATES) May 1997, 23 (5) p487-8, ISSN 0342-4642 Journal Code: H2J
Comment on Intensive Care Med 1997 May;23(5):504-9
Languages: ENGLISH
Document type: COMMENT; EDITORIAL

6/7/13 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

126263165 CA: 126(20)263165k PATENT
Anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
INVENTOR(AUTHOR): Haselbeck, Anton; Schumacher, Guenther; Co, Man Sung; Martin, Ulrich
LOCATION: USA
ASSIGNEE: Protein Design Labs, Inc.; Boehringer Mannheim Gmbh; Haselbeck, Anton; Schumacher, Guenther; Co, Man Sung; Martin, Ulrich
PATENT: PCT International ; WO 9706822 A1 DATE: 19970227
APPLICATION: WO 96US13152 (19960814) *EP 95112895 (19950817) *EP 95114696 (19950919) *US 578953 (19951227)
PAGES: 52 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A
DESIGNATED COUNTRIES: AL; AM; AU; BB; BG; BR; CA; CN; CU; CZ; EE; FI; GE; HU; IL; IS; JP; KG; KP; KR; LK; LR; LT; LV; MD; MG; MK; MN; MX; NO; NZ; PL; RO; SG; SI; SK; TR; TT; UA; US; UZ; VN; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM
DESIGNATED REGIONAL: KE; LS; MW; SD; SZ; UG; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA215003 Immunochemistry
IDENTIFIERS: monoclonal antibody selectin multiple organ failure
DESCRIPTORS:
DNA sequences... Extracorporeal circulation... E-selectin... Immunoglobulins... L-selectin... Monoclonal antibodies... Plasma(blood)... Protein sequences... P-selectin... Selectins... Serum(blood)...
anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Organ(animal)...
failure; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage

Antibodies...
humanized; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Organ(animal)...
injury, acute; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Diseases(animal)... Organ(animal)...
multiple organ failure; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Injury...
organ, acute; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Diseases(animal)...
organ failure; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
Trauma...
poly-; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage

CAS REGISTRY NUMBERS:

188763-45-3 188763-47-5 amino acid sequence; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage
188763-44-2 188763-46-4 nucleotide sequence; anti-selectin antibodies for prevention of multiple organ failure and acute organ damage